VOL. CLXVIII, No. 6 DECEMBER, 1924 No. 633

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

JOHN H. MUSSER, JR., M.D., EDITOR
E. B. KRUMBHAAR, M.D., ASSOCIATE EDITOR

THE LIBRARY OF CONGRESS SERIAL RECORD
JUL 26 1944

ESTABLISHED 1820

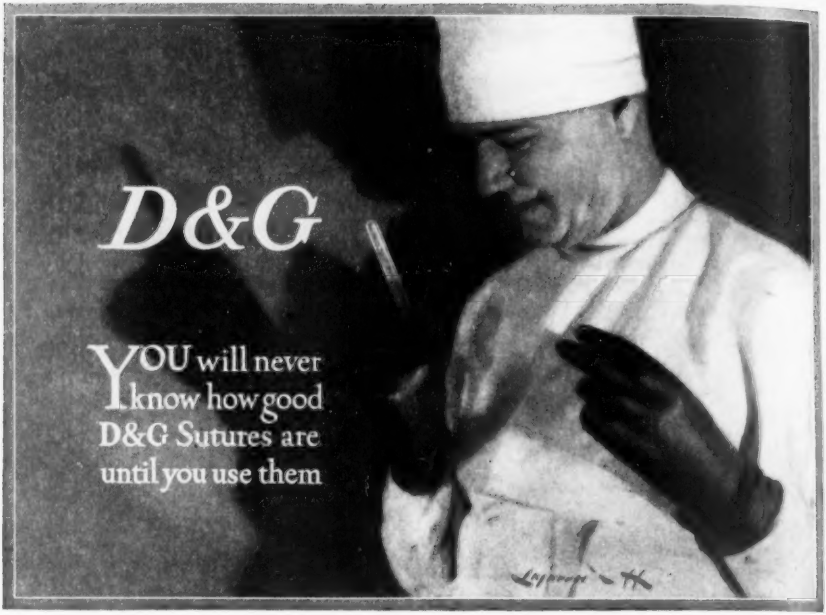
PROGNOSIS IN ORGANIC HEART DISEASE. By GEORGE W. NORRIS, B.A., M.D. . . . 781
THE PROGNOSIS OF ANGINA PECTORIS. By LOUIS HAMMAN, M.D. 786
PROGNOSIS OF THE TACHYCARDIAS. By JAMES S. McLESTER, M.D. 795
TUMORS OF THE BREAST: A CLINICAL CONSIDERATION. By JOHN F. ERDMANN, M.D. 799
THE RESULTS OF OPERATIONS FOR CHRONIC APPENDICITIS (SECOND SERIES). By CHARLES L. GIBSON, M.D. 807
THE PRESSURE FACTORS IN THE BILIARY-DUCT SYSTEM OF THE DOG. By A. WINKELSTEIN, M.D., and P. W. ASCHNER, M.D. 812
BONE MARROW AND SPLEEN IN THE TREATMENT OF ANEMIA. By CHAUNCEY D. LEAKE, Ph.D., and JOSEPH S. EVANS, M.D. 819
SPLENIC ANEMIA: REPORT OF A CASE IN A LATE STAGE CURED BY SPLENECTOMY. By EDMUND HORGAN, M.D., F.A.C.S., in collaboration with WILLIAM P. REEVES, M.D., F.A.C.S., and WILLIAM EARL CLARK, M.D., F.A.C.P. 836
COMBINED SCLEROSIS OF THE SPINAL CORD AND CARCINOMA OF THE STOMACH: REPORT OF A CASE. By JOHN L. GARVEY, M.D., and LOUIS D. STERN, M.D. . 847
THE TREATMENT OF TETANUS, WITH SPECIAL REFERENCE TO THE USE OF MAGNESIUM SULPHATE. By CARROLL SMITH, M.D., F.A.C.S., and W. E. LEIGHTON, M.D., F.A.C.S. 852
OBSERVATION OF FAT DIGESTION FOR CLINICAL STUDY AND PHYSIOLOGICAL DEMONSTRATION. By ANTHONY BASSLER, M.D., F.A.C.P., and J. RAYMOND LUTZ, B.S., M.D. 869
PRIMARY CANCER OF THE LIVER. By JULIUS FRIEDENWALD, M.D., and HIRAM FRIED, M.D. 875
THE PATHWAYS OF THE MEDIASTINUM, THE LUNGS, AND THE PLEURAE. By J. CURTIS LYTER, M.D. 882
A NEW VASCULAR SIGN OF DEATH. By MORRIS H. KAHN, M.A., M.D. 890
AURICULAR FLUTTER, WITH PERIODS OF 1 : 1 VENTRICULAR RESPONSE. By THOMAS M. McMILLAN, M.D., and JOHN A. SWEENEY, M.D. 893
INDEX TO ADVERTISERS . . . . . ADV. PAGE 38

Contents continued on page x

OWNERS AND PUBLISHERS
Philadelphia LEA & FEBIGER New York

COPYRIGHT, 1924, BY LEA & FEBIGER. ALL RIGHTS RESERVED. ENTERED AT THE POST-OFFICE AT PHILADELPHIA AS SECOND-CLASS MATTER

PUBLISHED MONTHLY. SUBSCRIPTION, SIX DOLLARS A YEAR, POSTPAID



Alterative
Analgesic

PANALGYN

Each fluidounce of Panalgyn contains Strontium Salicylate twenty grains, Strontium Iodide eight grains, Colchicine one fiftieth grain, Pilocarpine one eighth grain, Gelsemium one grain.

The disagreeable taste of the Salicylate and the Iodide is effectually disguised in an aromatic vehicle, so that Panalgyn will be found perfectly acceptable to the majority of patients.

Panalgyn is indicated in the treatment of acute and chronic rheumatism, lumbago and gout. It will also be found of value in sciatica, rheumatic neuritis and allied pathological conditions.

Sample supplied upon request.

SHARP & DOHME
BALTIMORE

New York Chicago New Orleans St. Louis Atlanta
Philadelphia Kansas City San Francisco

Ano

ILETI

Effe

Following the
ing prices as rap
Iletin (Insulin, Li

U-
U-
U-

This is
Compa
lowers

LESS

Ample

Iletin (

S

ELI

ontium Sal-
ight grains,
ighth grain,

the Iodide
cle, so that
ble to the

acute and
vill also be
and allied

tlanta

Another Price Reduction

ILETIN (INSULIN, LILLY)

Effective November 1st, 1924

Following the established custom of Eli Lilly and Company in reducing prices as rapidly and consistently as lower production costs permit, Iletin (Insulin, Lilly) is now offered to physicians at the following prices:

U-10 (50 units) in 5 c.c. vials-$ .50 per vial
U-20 (100 units) in 5 c.c. vials-$ .85 per vial
U-40 (200 units) in 5 c.c. vials-$1.55 per vial

SIXTH REDUCTION

This is the sixth reduction in price since Eli Lilly and Company first offered Iletin (Insulin, Lilly) for sale and it lowers the average cost to

LESS THAN ONE CENT PER UNIT TO THE PHYSICIAN

Ample supplies of Iletin (Insulin, Lilly) are available to meet any conceivable demand.

Iletin (Insulin, Lilly) is supplied through the Drug Trade

Send for file of pamphlets giving full information

ELI LILLY AND COMPANY

INDIANAPOLIS, INDIANA, U·S·A

Yeast

an established prescription of the general practitioner

ALTHOUGH for centuries yeast has been prescribed by physicians, it has been notably in the past seven years that scientific research has revealed new and extended fields for its use.

During this period exhaustive investigations have been carried out under independent authorities. In all, six separate groups of men have completed rigidly conducted tests and experimental work on the various phases of yeast's activity.

Summarized, the aggregate findings of the different groups of scientists engaged on this research work are as follows:

First: The water soluble B-vitamin, of which yeast is the richest source extant, raises the plane of metabolism rapidly and effectively — indicating yeast as a simple corrective for digestive troubles, and an extremely valuable dietary aid.

Second: By inducing a leucocytosis yeast provides a highly efficacious treatment of furunculosis and other skin disorders.

Third: The laxative action of yeast not only produces an increase in the bulk and moisture of the feces and (to quote the findings of the most recent investigation) an "improvement in the condition of every individual" with "any degree of constipation" but also acts as a natural, efficient bowel regulator without any drastic purgative action.

The combination of these three properties makes yeast a valuable prescription not only in cases of specific trouble but also in certain cases of vague ill health which require a restorative for the general tone of the system.

Fleischmann's Yeast can be taken dissolved in milk or fruit juices or eaten plain. A popular method of administration is one cake half an hour before breakfast and the last thing at night dissolved in a glass of water (just hot enough to drink).

New brochure on yeast therapy sent on physician's request

THE FLEISCHMANN COMPANY, Dept. K-38
701 Washington Street, New York.

Please send me free a copy of the brochure on yeast based on the published findings of distinguished investigators.

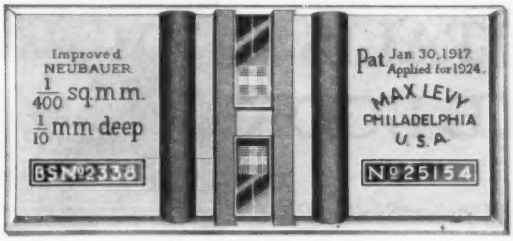
Name .....

Street .....

City ..... State .....

LEVY COUNTING CHAMBERS

WITH IMPROVED NEUBAUER RULING



No. 3311. (Actual Size.)

LEVY COUNTING CHAMBERS embody a greater accuracy as to depth of chamber and dimensions of ruling than any hitherto offered of either European or American manufacture. This statement is based on repeated measurements by unquestioned authorities. New features in the latest model are as follows:

IMPROVED NEUBAUER RULING

One-piece solid slide construction, with the ruling made directly on the glass slide, which obviates any possibility of separation between the slide and the ruled glass strip.

Outside or protecting trenches of greater width than formerly.

Transverse trench on the double cell of greater width than formerly.

A matte focusing surface and an indicating or finding line to facilitate immediate location of the ruled area in the microscope field without danger of disturbing the distribution and vitiating the count by touching the cover glass with the objective.

The polished surface bearing the ruling of smaller and standardized size, enabling a drop of uniform and minimum size to be used.

The ruling on LEVY COUNTING CHAMBERS consists of deep, permanent, sharply cut lines of a high degree of visibility throughout the entire range of focus necessary to count all the cells in a given field. Comparison of the degree of visibility of these rulings with that of other makes should always be made with the cells filled with diluting solution.

			Code Word
3300.	**Levy Counting Chamber,** with Improved Neubauer single ruling....	**$7.00**	*Czacu*
3301.	**ditto,** with Improved Neubauer double ruling.....	**10.00**	*Czapt*
3310.	**Certified Levy Counting Chamber,** with Improved Neubauer single ruling and Bureau of Standards' certificate	**10.00**	*Czoak*
3311.	**ditto,** with Improved Neubauer double ruling.....	**14.00**	*Czorb*
3350.	**American Standard Haemacytometer,** complete in case, with Levy Counting Chamber with Improved Neubauer single ruling.....	**14.00**	*Darip*
3351.	**ditto,** with Improved Neubauer double ruling.....	**17.00**	*Darvo*
3355.	**Certified American Standard Haemacytometer,** with Bureau of Standards' certification, complete in case, with Levy Counting Chamber with Improved Neubauer single ruling.....	**19.50**	*Dalpy*
3356.	**ditto,** with Improved Neubauer double ruling	**23.50**	*Daufs*

Copy of new descriptive pamphlet, "American Standard Haemacytometers," also circular regarding special sale of remaining stocks of discontinued rulings, sent on request

---

ARTHUR H. THOMAS COMPANY

RETAIL—WHOLESALE—EXPORT

LABORATORY APPARATUS AND REAGENTS

WEST WASHINGTON SQUARE **PHILADELPHIA, U. S. A.**

CABLE ADDRESS, "BALANCE," PHILADELPHIA

Leaves from a

DIGITALIS NOTE BOOK

No. XIII

By. F. A. Upsher Smith, Ph. C.

Thanksgiving

At this time of year "the song of harvest home" is heard throughout the land, alike in the cotton fields of Georgia and the wheat plains of the Dakotas.

In tune with this sentiment, we experience a feeling of gladness that our leaves of Minnesota digitalis are "safely gathered in," of prime quality and sufficient in quantity to carry us until the next harvest is due.

On account of the unusually adverse weather conditions that prevailed during the past summer, we are all the more thankful that the crop has proved ample for the coming year's needs.

Upsher Smith, Inc.
720 Washington Ave., S.E., Minneapolis, Minn.

Gastron

The entire-stomach-gland extract

Submitted to the physician as a resource against gastro-intestinal affections.

GASTRON presents the enzymes, complex proteins, coagulable and non-coagulable, the nucleo-proteins, amino-acids, etc., derivable from the gastric mucosa.

Agreeable solution—no sugar, no alcohol.

Fairchild Bros. & Foster
New York

Experience in private practice has demonstrated that in addition to the usefulness of TOLYSIN in treating rheumatism, its analgesic, antipyretic and decongestive properties are of value in treating coryza, tonsillitis, arthritis of gonorrheal origin, sub-acute rheumatism, symptomatic headaches and neuralgias.

TOLYSIN is usually prescribed 2–3 tablets (10–15 grains) three to four times daily with water.

Literature upon request.

THE CALCO CHEMICAL COMPANY

Calco

Pharmaceutical Division

Works at
Bound Brook, N. J.

New York Office
136 Liberty Street

~Its wide usage is an expression of its efficiency~

DIGALEN

The Well Known Digitalis

The Hoffmann-La Roche Chemical Works, New York
Makers of Medicines of Rare Quality

CÉLESTINS
VICHY

The place of CÉLESTINS Vichy in the dietary is distinctive and important. It is an alkaline water of diuretic action, and is indicated in cases of the following:

Chronic hepatic disorders; gastric and intestinal indigestions; acid dyspepsia; chronic catarrhal gastritis or enteritis; rheumatism; diabetes; inflammation of the bladder; and a large number of minor ailments.

CÉLESTINS VICHY is bottled only at Vichy, France, under the direct supervision of the French Government. Order and insist upon getting CÉLESTINS VICHY.

A booklet on the therapeutic uses of CÉLESTINS Vichy will be sent on request.

HENRY E. GOURD

General Distributor

456 Fourth Avenue **New York City**

New Castle Incubator

CASTLE

Chamber has uniform and constant temperature

THE new Castle Incubator fills the need for a reliable and accurate apparatus at a moderate price.

The electric heater is beneath the bottom (not taking up space in the chamber). It distributes the heat uniformly from the bottom to the top and maintains an unvarying temperature.

The automatic regulator controls the escape of excess heat up and out through the rear double wall. The walls are made of thick insulating material, bound with polished copper.

Send for details and prices

CASTLE

Sterilizers and bacteriological apparatus

Wilmot **Castle Co., 1160 University Av., Rochester, N. Y.**

D.R.L.

Superior Arsphenamines

Why do eminent syphilologists prefer and use D. R. L. Arsphenamines? It is because of their superior quality, wide margin of safety and high therapeutic efficiency.

D. R. L. were the first American Arsphenamines. No others furnish to such a degree this desirable combination of "Safety First and Quality Always."

Ask your dealer for these proven products and always specify D. R. L.

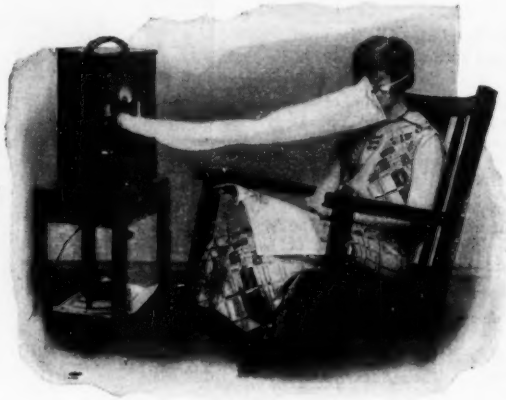
ARSPHENAMINE, D. R. L. NEOARSPHENAMINE, D. R. L.
SULPHARSPHENAMINE, D. R. L.
POTASSIUM BISMUTH TARTRATE, D. R. L. METAPHEN, D. R. L.

THE DERMATOLOGICAL RESEARCH LABORATORIES
1720-1726 Lombard Street, Philadelphia

Branch of
THE ABBOTT LABORATORIES
4753 Ravenswood Avenue, Chicago

NEW YORK SEATTLE SAN FRANCISCO LOS ANGELES TORONTO

Accurate Chlorine Concentration



THE remarkable results of Vedder and Sawyer (Jour. A.M.A., March 8, 1924) in the treatment of respiratory diseases with chlorine gas were secured in a constant flow chamber at Edgewood Arsenal where their experiments were conducted.

Fresh air entered the chamber constantly—and each portion of air had precisely the proper amount of chlorine to give the desired concentration of fifteen millionths of a gram per litre.

The W&T Chlorine Inhalator duplicates *for individual treatment* the conditions that existed in the constant flow chamber. It maintains the exact concentration required throughout the hour of treatment.

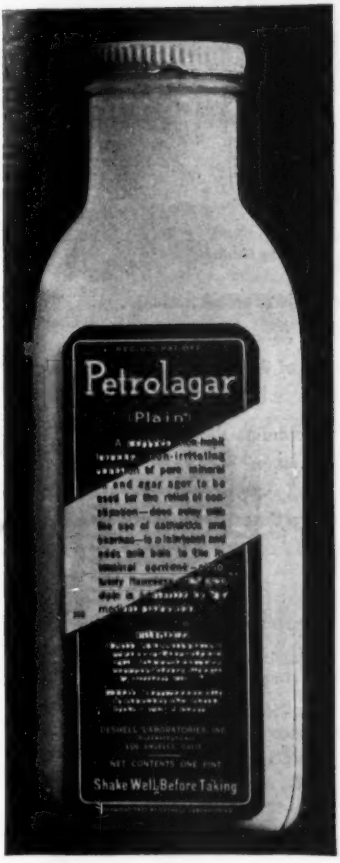
Technical Publication No. 61 gives full details.
Write for a copy.

WALLACE & TIERNAN
COMPANY, INCORPORATED
Manufacturers of Chlorine Control Apparatus
NEWARK NEW JERSEY

4

Petrolagar

(Trade Mark)



IN POST-OPERATIVE TREATMENT

In post-operative cases, PETROLAGAR is being found of particular benefit, administered just as soon as the patient can tolerate anything in the stomach after the operation, PETROLAGAR produces what might be termed a "passive peristalsis," and a bland, easy bowel movement.

PETROLAGAR is offered as a solution of the problem of keeping the bowel open for two or three weeks after the operation in an effective manner, without the creation of the cathartic habit.

PETROLAGAR is an emulsion of pure paraffin base mineral oil of the highest specific gravity and viscosity, with agar-agar which combination provides both lubrication and bulk to promote peristalsis.

It has a smooth, non-irritating action—the oil lubricating, and the agar adding a bland, soft bulk, which produces peristalsis without irritation or discomfort.

The possibility of leakage is reduced to a minimum, and there is no oily or unpleasant taste.

PETROLAGAR is issued as follows:
PETROLAGAR (Plain);
PETROLAGAR (with Phenolphthalein);
PETROLAGAR (Alkaline) and
PETROLAGAR Unsweetened (no sugar).

Use this coupon for a clinical trial specimen

DESHELL LABORATORIES, Inc.

3064 West Pico St., LOS ANGELES *Dept. J.* **589 East Illinois St., CHICAGO**

Mail to the Nearest Address

Deshell Laboratories, Inc., Dept. J.

GENTLEMEN:

Please send me a clinical specimen of

.....PETROLAGAR (Plain)
.....PETROLAGAR (with Phenolphthalein)
.....PETROLAGAR (Alkaline)
.....PETROLAGAR Unsweetened (no sugar)
(Mark type desired)

Dr. .....

Address.....

.....

CONTENTS

ORIGINAL ARTICLES

Prognosis in Organic Heart Disease 781
By George W. Norris, B.A., M.D., Philadelphia.

The Prognosis of Angina Pectoris 786
By Louis Hamman, M.D., Baltimore, Md.

Prognosis of the Tachycardias 795
By James S. McLester, M.D., Birmingham, Ala.

Tumors of the Breast: A Clinical Consideration 799
By John F. Erdmann, M.D., New York.

The Results of Operations for Chronic Appendicitis (Second Series) . . 807
By Charles L. Gibson, M.D., New York.

The Pressure Factors in the Biliary-duct System of the Dog 812
By A. Winkelstein, M.D., and P. W. Aschner, M.D., New York.

Bone Marrow and Spleen in the Treatment of Anemia 819
By Chauncey D. Leake, Ph.D., and Joseph S. Evans, M.D., Madison, Wis.

Splenic Anemia: Report of a Case in a Late Stage Cured by Splenectomy 836
By Edmund Horgan, M.D., F.A.C.S., in collaboration with William P. Reeves, M.D., F.A.C.S., and William Earl Clark, M.D., F.A.C.P., Washington, D.C.

Combined Sclerosis of the Spinal Cord and Carcinoma of the Stomach: Report of a Case 847
By John L. Garvey, M.D., and Louis D. Stern, M.D., Ann Arbor, Michigan.

The Treatment of Tetanus, with Special Reference to the Use of Magnesium Sulphate 852
By Carroll Smith, M.D., F.A.C.S., and W. E. Leighton, M.D., F.A.C.S., St. Louis, Mo.

Observation of Fat Digestion for Clinical Study and Physiological Demonstration 869
By Anthony Bassler, M.D., F.A.C.P., and J. Raymond Lutz, B.S., M.D., New York.

(*Contents continued on page 12*)

NEW YORK SKIN AND CANCER HOSPITAL

Alumni New York Skin and Cancer Hospital Graduates of this Post-Graduate School are requested to send their present professional office address to the secretary of the reorganized Alumni Association.

DR. HERMAN GOODMAN
15 Central Park West, New York City

ORGANOTHERAPY

can be effective only through the use of dependable endocrine products. A proper manufacturing process is absolutely indispensable.

"• • • every link in the manufacture of the glandular substance plays a vital part in its future therapeutic value, every stage in its production counts in its efficiency. It may become either a dangerously potent weapon or an inert mass." — ("Our Problems in Endocrinology," Jacob Gutman, M.D., Phar.D., F.A.C.P., Chairman's address to the Endocrinological Society of the City of New York, 1922.)

Our products are prepared from fresh glands of healthy food animals in our own laboratory, under the supervision of our own staff of chemists. Every manufacturing process has been carefully tested and every product for which there is a recognized chemical or biological assay is analyzed and standardized.

EPINEPHRINE
EPINEPHRINE CHLORIDE SOL.
DESICCATED PITUITARY BODY, U. S. P.
DRIED SUPRARENALS, U. S. P.
DRIED THYROIDS, U. S. P.
SOLUTION OF POST-PITUITARY
CORPUS LUTEUM
PANCREATIN, U. S. P.

Insure potency and constancy of action by prescribing the products of

G. W. CARNRICK CO.

Manufacturers of G.W. CARNRICK CO. **Organotherapeutic Products**

417-421 Canal Street, New York, N. Y.

Primary Cancer of the Liver 875
By Julius Friedenwald, M.D., and Hiram Fried, M.D., Baltimore, Md.

The Pathways of the Mediastinum, the Lungs, and the Pleuræ . . . 882
By. J. Curtis Lyter, M.D., St. Louis, Mo.

A New Vascular Sign of Death 890
By Morris H. Kahn, M.A., M.D., New York.

Auricular Flutter, with Periods of 1 : 1 Ventricular Response 893
By Thomas M. McMillan, and John A. Sweeney, Philadelphia.

REVIEWS

Handbook of Skin Diseases. By Frederick Gardiner, M.D. 902
The First Century of the Philadelphia College of Pharmacy. Edited by Joseph W. England 902
Insulin in General Practice. By A. Clarke Begg, M.D., O.B.E., Ch.B., M.B. 902
The Medical Department of the United States Army in the World War. Washington: Government Printing Office 903
The Foundation of Health. By William Barnard Sharp, S.M., M.D., Ph.D. 903
The Human Testis and Its Diseases. By Max Thorek, M.D. . . . 904
A Record of Measurements, Weights, and Other Facts Relating to Man. The William Ramsey Henderson Trust Reports Nos. 2 and 3. By J. F. Tocher 904
Modern Methods of Treatment. By Logan Clendening, M.D. . . . 905
The Romance of a Living Temple: A Study of the Human Body. By Frederick M. Rossiter, B.S., M.D., L.C.R.P., M.R.C. 905
General Cytology. Edited by E. V. Cowdry 906
Artificial Limbs: Appliances for the Disabled. By Dr. Florent Martin . 906
Clinical Aspects of the Electrocardiogram. By Harold R. B. Pardee, M.D. 907
Diseases of the Eye. By Charles H. May, M.D. 907
Protoplasmic Action and Nervous Action. By Ralph S. Lillie . . . 908
Anesthesia in Dental Surgery. By the late Thomas D. Luke, M.D., F.R.C.S. (Edin.). Edited by J. Stuart Ross, M.D., F.R.C.S. (Edin.) 908

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

Exsanguination,transfusion. A New Therapeutic Measure in the Treatment of Severe Toxemias 909
The Effect of Iodin in Exophthalmic Goiter 909
The Nasal Accessory Sinuses in Cardiopathies 910
The Ex-service Man and His Lungs 910

(*Contents continued on page 14*)

Serobacterins

(Antibody-Antigens)

Serobacterins are sensitized bacterial vaccines—antibody-antigen combinations.

Sensitized bacterial vaccines are a development of the researches of Besredka and Metchnikoff, in the Pasteur Institute, Paris.

As a result of further research in the Mulford Biological Laboratories, serobacterins have now been made definite antibody and antigen combinations, which, on injection, impart at once a degree of passive immunity, followed by an active immunity.

The degree of immediate passive immunity is dependent on the amount of specific antibodies carried by the serobacterin and promptly liberated when injected into the body. Because of this immediate immunity, which saves valuable time, and because they cause less local and general reactions, Serobacterins are preferred to the ordinary non-sensitized bacterins by many physicians, for both preventive and curative treatment.

Ask for Mulford Working Bulletin No. 18 62020

H. K. MULFORD COMPANY, PHILADELPHIA, U. S. A.

Mulford

THE PIONEER BIOLOGICAL LABORATORIES

LISTERS

PREPARED CASEIN

DIABETIC FLOUR

STRICTLY STARCH FREE

Diabetic Non-Carbohydrate

Muffins
Biscuits
Bread
Cookies
Pancakes
Pastry

The Physician prescribes the Flour—the patient easily makes the foods.

These palatable and hunger-satisfying foods are easily made in any home from LISTERS prepared casein DIABETIC FLOUR (self-rising.) A month's supply carton (30 boxes of Flour)—$4.85, or fifteen days supply carton (15 boxes) $2.75. Easily followed recipes for making more than twenty palatable and attractive (starch-free) foods come in each carton. Sent direct to your patient or the address of nearest agency given on request.

Accepted by the Council

LISTER BROTHERS, Inc.

405 Lexington Avenue :: :: NEW YORK CITY

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

Intra-abdominal Biliary Exclusion from the Intestines—Cholecystitis—Nephrostomy—A New Method 911
Mortality from Empyema in Children 912
Subcutaneous Tenotomy of the Tendon of Achilles 912
Treatment of Bone and Joint Tuberculosis 912
The Dangers of Unabsorbable Sutures in Gastroenterostomy 913
Surgery of the Knee-joint 913
Chronic Stenosis of the Duodenum 913
The Etiology of the Femoral Hernial Sac 913

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Contraindications to the Use of Digitalis in Certain Types of Cardiac Insufficiency 914
Constipation of Civilization and its Treatment with Substances which Increase the Bulk of Feces, Particularly Normacol 914
The Precipitation of the Crisis in the Treatment of Pneumonia 915

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.

Mental Health Problems in School Children 915
The Intravenous Use of Mercurochrome-220 Soluble in the Treatment of Pneumonia in Children 916
The Effect of the Routine Administration of Cod-liver Oil on the Development of Rickets in the Breast-fed 917
Clinical Studies of Some Diseases of the Blood in Children with Illustrative Cases 917
A Clinical Study of Lactic Acid Milk as a Routine Feeding for Sick and Healthy Infants 918
Medical Aspects of Acute Appendicitis in Children 918

(*Contents continued on page 16*)

BROMURAL

Soothes the *Nerves* and Induces *Refreshing* Sleep

In powder and 5-grain tablets

Dose: 1 to 3 Tablets.
Literature and samples from **E. BILHUBER, Inc., 25 West Broadway, New York City**

Liquid Peptonoids with Creosote

has been demonstrated to be a thoroughly dependable product.

It combines the active *and* known therapeutic qualities *of* Creosote *and* Guaiacol, with the nutritive properties *of* Liquid Peptonoids.

It is extremely agreeable to the palate *and* acceptable to the stomach.

The peculiar ability *of*

Liquid Peptonoids with Creosote

to check a persistent, "hang-on" Winter cough—should be remembered.

It acts as a broncnial sedative and expectorant.

SAMPLES ON REQUEST

THE ARLINGTON CHEMICAL COMPANY
YONKERS, N. Y.

For Accuracy in Diagnosis

use genuine "E. S. I. Co." Electrically Lighted Instruments

The Ninth Edition of our Catalogue

describes and illustrates our complete line of instruments, designed both for the work of the specialist and of the general practitioner. A copy will be mailed upon request.

To obtain proper service from our instruments, make certain you are using genuine "E. S. I. Co." lamps. For your convenience in ordering correct lamps, write for a copy of our Lamp Sheet.

Our twenty-five years of service to the Medical Profession and the fact that our instruments are made in accordance with the suggestions and with the co-operation of the eminent physicians and surgeons whose names they bear, is the best guarantee of their satisfactory character.

Nasopharyngoscope—*Holmes.*
Transilluminators—*Sullivan.*
Bronchoscopic Instruments—*Jackson, Lynah.*
Cystoscopes — *Braasch, Young, Kelly, E. S. I. Co.*
Urethroscopes — *Swinburne, Young, Gordon, Koch, MacGowan, Ballenger.*
Rectal Instruments — *Tuttle, Lynch, Axtell, Bassler, Beach, Buie.*

Illuminated Eye Spud, Nasal Snare, Mouth Gag, Vaginal Specula, Rectal Specula.

Auriscopes, Nasal Specula, Tongue Depressors, Laryngoscopes.

Tungsten Batteries.

Socket Current Controllers.

Cautery Transformers.

For your protection see that instruments are marked "E. S. I. Co."

Electrically Lighted Surgical Instruments

Electro Surgical Instrument Company
ROCHESTER, N. Y.

CONTENTS—(*Continued*)

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

JOHN H. STOKES, M.D.

The Treatment of Syphilis from an Experimental Point of View . . . 919
Treatment Results in Early Syphilis 921
The Problem of Arsphenamin Resistant Syphilis 921

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Cesarean Section for Occlusion of the Vagina and Calculus 922
The Sheppard-Towner Act 922
The Relation of Veneral Disease to Childbirth 923

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D., AND FRANK B. BLOCK, M.D.

Significance of Hematuria 924
Operative Results in Cervical Cancer 924
Treatment of Uterine Fibroids 925

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M., AND DE WAYNE G. RICHEY, B.S., M.D.

Properties of Purified Dick Scarlatinal Toxin 926
Kidney Changes in Pyloric Obstruction 926
Certain Pathological Tissue Changes in Thyroidectomized Sheep . . . 927
The Effect of Digestive Juices on the Potency of Botulinus Toxin . . 927

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND GEORGE W. McCOY, M.D.

Life Tables for the Population of New York State According to Nativity 928
Occurrence of Leptospira Icterohemorrhagiæ in Wild Rats of Baltimore 928
The Biseasonal Prevalence of Infantile Paralysis (Acute Anterior Poliomyelitis) 929
The Relations between a Carnivorous Diet and Mammalian Infections with Intestinal Protozoa 929
The Protection of Dogs against Rabies by Umeno's Method of Preventive Inoculation 929

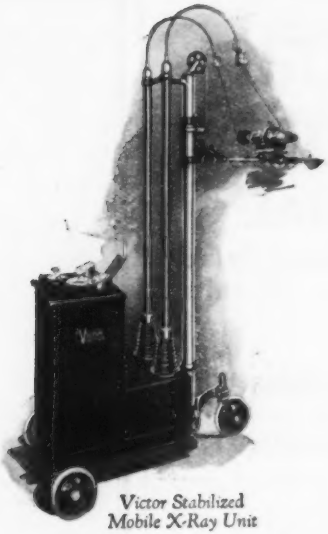
DIONIN ETHYLMORPHINE HYDROCHLORIDE MERCK

Cough Sedative

In respiratory affections

Asthma, Bronchitis, Pertussis

Merck & Co., New York



Victor Stabilized
Mobile X-Ray Unit

X-Rays and Professional Reputation

The professional success of the practitioner is in part dependent upon his office equipment. If it has been bought solely on its proved record, if it comes from a manufacturer who lives up to medical and not merely commercial standards it will maintain and even heighten a well-earned professional reputation.

Conscious of its obligations to the medical profession, the Victor X-Ray Corporation spends large sums in research which reveals new technical principles and which results in X-Ray apparatus of the highest medical standard. It realizes that not only the physician's patients must be considered, but also the professional reputation of the physician himself.

Victor Stabilized Mobile X-Ray Unit

The outfit which solves the problem of selecting the most practical and compact X-Ray apparatus for the physician's office. It is a complete, self-contained unit incorporating the Victor-Kearsley Stabilizer—an exclusive Victor feature—which standardizes technique and insures good radiographs consistently. This Stabilizer is one of the most important X-Ray developments in the last decade, having made possible the wider use of X-Rays by physicians, thru greatly simplified control and uniform results.

Note the large rubber-tired casters which make it a truly mobile outfit, easily shifted around the room.

Hospitals, too, are supplementing their stationary X-Ray equipment with this Mobile Unit, finding it ideal for bedside work in cases where the patient cannot be conveniently moved to the X-Ray laboratory.

VICTOR X-RAY CORPORATION, 236 South Robey Street, Chicago, Ill.

Sales Offices and Service Stations in All Principal Cities

VICTOR

Neutral Acriflavine NATIONAL

—one of the National Medicinal Products

A powerful antiseptic of unusual properties

NEUTRAL Acriflavine (National) has been used with success in the treatment of influenza, endocarditis, erysipelas, Ludwig's angina, acute pyelitis, and acute arthritis.

Unquestionably, Neutral Acriflavine (National) is an antiseptic worthy of your consideration. Let us send you the literature.

Pharmaceutical Division

National Aniline & Chemical Co., Inc.

40 Rector Street, New York, N. Y.

Pharmaceutical Division
National Aniline & Chemical Company, Inc.
40 Rector Street, New York

Please send me your booklet on "Neutral Acriflavine and Acriflavine," containing complete bibliography, clinical reports, etc.

Name .....

Professional Address ..... A.J.M.S. 12-24

IN

TETANUS, CHOREA

AND

CONVULSIONS

Eclamptic—Toxic

VEN-MAGNESIUM SULPHATE

2 cc. 25%

Intramuscular, subcutaneous, intravenous, intraspinal

IS INDICATED AS

RELAXANT, SEDATIVE

"Everything in Ampoules"
Write for Catalog

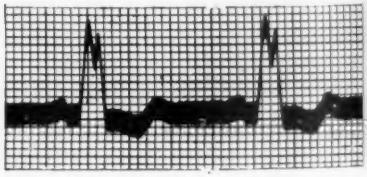
THE INTRA PRODUCTS CO.

Box 61, South
Denver, Colo.

"ELECTROCARDIOGRAPHY

Furnishes definite, indisputable evidence of structural heart muscle defect that is impossible of determination by any other method of examination."

S. CALVIN SMITH



Normal (sinus) rhythm. Rate 70. Left ventricular preponderance. Intra-ventricular heart block. P–R–P. 14 to 0.16 seconds. QRS–0.11 to 0.12 seconds. From a man, aged 45 years, with paroxysmal auricular fibrillation and attacks of precordial pain.

Practitioners, clinics and hospitals find it essential for a complete examination and the returns capable of creating its own maintenance fund besides allowing a generous surplus each year.

Catalog and details on request

CAMBRIDGE INSTRUMENT Co INC

MAIN OFFICE AND FACTORY OSSINING-ON-HUDSON NEW YORK | INCORPORATING CHAS. F. HINDLE | SALES OFFICE & SHOWROOM GRAND CENTRAL TERMINAL NEW YORK CITY

Palliate Pain with Peralga

– the Non-Narcotic Analgesic Sedative

PERALGA

Partial and frequently a complete substitute for Morphine and other Opiates.

For the symptomatic treatment of "Headaches" due to menstrual and climacteric disorders, nervous conditions, hysteria, mental exhaustion, migraine, hemicrania, eye-strain.

A material aid in the management of dysmenorrhea and menorrhalgia; pains of locomotor ataxia, of the acute gall-stone attack, of malignant tumors; traumatic pain, post-operative or from injury; drug addiction and insomnia due to pain.

Furnished in

Tablets, **3 grains, Tins of twelve and Bottles of one hundred.**

Powder, **Bottles of one ounce and half-ounce.**

Information and Trial Material from

SCHERING & GLATZ, INC.

150-152 MAIDEN LANE
NEW YORK

705 UNITY BUILDING
MONTREAL

Manufacturing Laboratories: BLOOMFIELD, N. J.

The Trade Mark "PERALGA" is registered the U. S. Pat. Off. under No. 160960.

IN THE COURSE OF MANUFACTURE

Of

OVARIAN GLANDULAR PRODUCTS

there are many opportunities for injuring the active therapeutic constituents, and there is, therefore, considerable variation in the potency of the different makes of these products. It has been our aim to present desiccated substances representing as nearly as possible the gland or the respective part of the gland as found in the animal itself and to eliminate operations likely to injure or alter the active principles.

LUTEIN—corpus luteum—TABLETS, H. W. & D.
WHOLE OVARY TABLETS, H. W. & D.
OVARIAN RESIDUE TABLETS, H. W. & D.

are dried in vacuo
and are not treated with solvents

in our process of manufacture. Our drying methods make it possible to desiccate the glandular materials below animal body heat, which eliminates the probably injurious effects of high temperatures. The fact that solvents are not used does away with the possibility of extracting potent agents with such solvents.

AS THERE IS NO OPPORTUNITY OF DESTROYING OR REMOVING ACTIVE CONSTITUENTS, THE UNALTERED FRESH GLANDULAR MATERIAL SHOULD BE REPRESENTED BY OUR DESICCATED TABLETS

H. W. & D.—Specify—H. W. & D.—Specify—H. W. & D.—Specify—H. W. & D.

HYNSON, WESTCOTT & DUNNING, Baltimore, Md.

Toxin-Antitoxin (LEDERLE)

For Immunization against Diphtheria

Park conclusively demonstrated the value of diphtheria immunization with Toxin-Antitoxin Mixture. Immunity still persists in over 90% of children immunized six years ago.

Toxin-Antitoxin (LEDERLE) is made according to Park's modified formula, containing one-tenth L plus dose of toxin.

Studies during the past two years show that no severe reactions followed the use of this modified formula either in children or adults. This product therefore permits of universal immunization against diphtheria.

LEDERLE ANTITOXIN LABORATORIES

NEW YORK

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

DECEMBER, 1924

ORIGINAL ARTICLES.

PROGNOSIS IN ORGANIC HEART DISEASE.*

By George W. Norris, B.A., M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; CHIEF OF MEDICAL SERVICE AT THE PENNSYLVANIA HOSPITAL.

Prognosis. In venturing a prognosis our view must be taken with a large background of perspective and not from a narrow field focussed upon the heart alone. More or less prolonged observation is usually necessary. A single examination, no matter how searching and complete, is apt to lend too much support to David's despairing dictum that "all men are liars." Our bodement must also include a careful inquiry into symptomatology. An answer to the question "What can he do?"—without fatigue, pain, dyspnea, cough, cyanosis or edema—will shed the light of truth upon many a doubtful case. Recurrent attacks of decompensation, especially if unprovoked, are of bad augury, and opinion should be withheld if the patient is seen for the first time while decompensation obtains. The age of the patient also has a bearing. If the disease develops in early adult life, the outlook is more promising than if it appears earlier or later, because the strain of growth is over, the likelihood of renewed infection is lessened, disease of other organs has not yet begun and degenerative arterial changes are still in the future.

We should bear in mind that factors which bring about cardiac decompensation are the same factors which cause death. They are four in number, their relative importance being in the order named: (1) Infection; (2) arteriosclerosis; (3) change of rhythm; (4) toxemia.

* Read before the American Climatological and Clinical Association, May, 1924. (Angina Pectoris and the Tachycardias were discussed by other speakers.)

Social surroundings play an important role. A change of occupation may greatly change our predictions. "In youth the family history, in adult life the habits, and in later years the circumstances, should be carefully scrutinized." (Cowan.) The patient's temperament is often a factor of great importance. Finally the response to treatment—the ease with which compensation is established by rest, underfeeding and digitalis gives us still further clues as to the degree of myocardial impairment.

Remember that the *effort syndrome* engrafted upon an organic lesion may produce symptoms which unless recognized and properly evaluated may render prognosis erroneously austere.

Prognosis will depend largely upon etiology. We no longer consider our cases as aortic insufficiency or mitral stenosis but rather as "mitral disease rheumatic with probably stenosis or aortic disease syphilitic, late," etc. In a similar manner we must properly classify the lesions primarily due to arteriosclerotic, renal or endocrine disturbances before venturing a prophecy.

Blood-pressure. In some cases of organic heart disease blood-pressure may have considerable prognostic significance. This applies chiefly to older individuals with myocardial rather than valvular lesions. Constantly high readings, especially of the diastolic pressure, indicate the degree of muscular strain to which the heart is constantly subjected and point strongly to renal lesions or other unknown toxic factors. This is generally recognized but it is worth while remembering that life insurance statistics indicate that 140/94 mm. represents the upper normal limit rather than 160/100 mm., which is generally accepted as the physician's standard. How greatly increased pressure above the expected normal influences the mortality rate will be seen in the accompanying table which shows, that an increase of from 25–34 mm. doubles and of + 50 mm. quadruples the death-rate. Abnormally low pressure on the other hand favors longevity, except in cases where it represents the terminal fall of an antecedent higher pressure. It has been estimated that including deaths from all causes the mortality of individuals with a pressure below 100 mm. was 65 per cent less than that expected.*

Sudden deaths occur in angina pectoris, in some aortic lesions and occasionally in mitral disease (from embolization or ventricular fibrillation). With these exceptions death from heart disease is usually a slow and torturing process. It is in my opinion also a fact that even in the absence of the first mentioned well-known causes, unexpected and unexplained arrest of heart action may result from purely reflex nerve influences. Sudden deaths, followed by careful autopsies with negative findings—we have all of us seen.

* Fisher, J. W.: Further Report of the Diagnostic Value of the Systolic and Diastolic Blood-pressure, Assn. Life Ins. Med. Directors, 1921.

SUMMARY OF THE MORTALITY EXPERIENCE OF THE NORTHWESTERN MUTUAL LIFE INSURANCE COMPANY, WITH RESPECT TO THE

3104C1
19 Jy 44

SUMMARY OF THE MORTALITY EXPERIENCE OF THE NORTHWESTERN MUTUAL LIFE INSURANCE COMPANY, WITH RESPECT TO THE PALPATORY SYSTOLIC AND AUSCULTATORY DIASTOLIC BLOOD-PRESSURE.

Years of entry.	Range arterial tension.	Ages at entry.	Number of Lives. Accepted.	Number of Lives. Rejected.	Actual deaths.	Ratio actual to expected mortality (American men table). 100 per cent.* 200 per cent. 300 per cent. 400 per cent. Per cent.
1912–1920	Low blood-pressure 100 mm. and less	16–60	3389		26	**35.0
1915–1920	Diastolic blood-pressure 95 mm. and over	16–60	1244		22	78.6
1907–1910 to anniversary in 1919	Blood-pressure average 142 mm.	40–60	2610		310	94.0
	Blood-pressure average 153 mm.	40–60	520		90	114.4
Risks Rejected for High Blood-pressure Only. Years 1907–1920—Mortality Computed to Anniversity 1921 — *High Systolic Blood-pressure by Ages.*		16–29		743	18	195.7
		30–39		731	34	259.5
		40–49		1196	181	334.6
		50–60		1495	274	190.8
	Total	16–60		4165	507	230.5
	Mm. over Average Systolic Blood-pressure for Age. *Mm.* +10–14			525	26	136.1
	+15–24			1685	125	183.8
	+25–34			909	111	204.4
	+35–49			657	121	248.5
	+50			389	124	414.7
	Total	16–60		4165	507	230.5

* The Northwestern Mutual Life Insurance Company's General Mortality Experience about 80 per cent of the Table. ** Estimated Mortality.

Rheumatic Endocarditis. Prognosis during an initial attack is good if, as is usually the case, the disease becomes arrested and if the original focus of infection can be found and eliminated. A much more difficult point to decide is, has the process become arrested? For this we must rely upon the absence of fever, increased pulse-rate, leukocytosis, anemia and precordial sensations. Needless to add, each recurrence of the infection increasingly favors a subsequent one, and each such attack tends to cripple the heart more and more. Again, the longer the infection remains clinically recognizable the worse the outlook. So too, the more valves demonstrably involved, the worse the prognosis.

In the quiescent stage, when presumably the patient has no longer an infection, but merely a mechanical handicap to withstand, prognosis depends upon the antecedent myocardial damage, the life the patient leads, and the type of valvular lesion. Other factors being equal, mitral stenosis[1] is worse than aortic insufficiency and the latter far worse than mitral regurgitation. It cannot, however, be too much emphasized that it is the infection of the myocardium that counts. To a good heart muscle the particular valve involved makes relatively little difference. "Une maladie des valvules, ce n'est pas une maladie du coeur." What has been stated regarding the endocardium applies also to the pericardium. A pericardial effusion rarely causes death—it is the infection that kills. Pericardial adhesions may be a handicap, but it is the underlying fibroid myocarditis that brings the break in compensation.

In regard to acute and subacute (non-rheumatic) bacterial endocarditis, the prognosis is quite different. In the former condition death usually occurs within a month. In the subacute—frequently streptococcus viridans—type of infection the disease may masquerade as nephritis, pernicious anemia, meningitis or pneumonia, and so forth, and a correct diagnosis may be established only at autopsy. Intermissions—bacteria-free stages—are common and sometimes of long duration. Recoveries sometimes occur.

Syphilitic Cardiovascular Disease. In the first and second stages prognosis is good unless specific resistance to arsphenamin is present. This is even so in cases in which cardiac drugs alone have shown but little benefit. If, however, the combined treatment yields but little relief, the ultimate prognosis as to further improvement or cure is definitely bad (Brooks). Relapse after marked improve-

[1] Willus, F. A.: Life Expectancy with Mitral Stenosis: The cardiac mortality with mitral stenosis in Willius' series of cases was as follows: Complete series, 470 cases, cardiac mortality, 36.8 per cent after an average of 15.7 months. Mitral stenosis with auricular fibrillation, 116 cases, cardiac mortality 56.6 per cent after an average of 22.8 months. Mitral stenosis with presystolic or diastolic apical murmur, 253 cases, cardiac mortality 29.0 per cent after an average of 17.1 months. Mitral stenosis with presystolic or diastolic and apical systolic murmur, 197 cases, cardiac mortality 45.5 per cent after an average of 13.7 months. Significant *T* wave negativity, 50 cases, cardiac mortality 62.5 per cent after an average of 12.1 months. Ann. Clin. Med., 1923, **1**, 326.

ment is prognostically bad. Arrhythmia uncontrolled or with but little improvement has also an ominous augury. We must assume a permanent myocardial injury in all tertiary cases and advise accordingly.[2] In the tertiary stage arsphenamin and mercury are evanescent in effect. The danger of a Herxheimer reaction necessitates small doses and hence long treatment. Eradication of the spirochetes in their protected position is difficult. Nearly 70 per cent of Longcope's cases died within two years.[3] Seventy-five per cent of all cases of aortic insufficiency in adults are syphilitic. Eighty per cent of these occur in men. Among untreated cases 30 per cent develop aneurysms. Thirty per cent have retracted valves and as a rule attention arresting symptoms appear about fifteen years after the initial infection.

Clinical Arrhythmia. *Premature contractions* (extrasystoles) have *per se* little prognostic significance. Occurring as they commonly do as a result of diverse reflex causes their seriousness is estimated by the basic heart condition. To this statement, there is, however, one notably exception. When they occur in combination with auricular fibrillation the mortality is almost as high as that of alternation.

Heart-block (*auriculoventricular*) when present to a degree which can be demonstrated without the electrocardiogram, is extremely serious. A few cases of the Adams-Stokes syndrome have been known to recover and live for years after severe and prolonged attacks. But there are many cases of non-convulsive block, which occur in lesser degree in association with rheumatic and other heart lesions, which, even while persistent, are compatible with prolonged though restricted life. The therapeutic block which digitalization produces in auricular fibrillation belongs to this group.

Alternation of the pulse is usually a forerunner of the end. Nearly 100 per cent of White's cases[4] died within three years. I quite concur with Lewis[5] who, classing it with subsultus tendinum and risus sardonicus describes it as "the faint cry of an anguished and fast failing muscle, which, when it comes, all should strain to hear, for it is not long repeated. A few months, a few years at most, and the end comes."

[2] Brooks and Carroll: Treatment of Heart Involvement in Syphilis, 300 Cases, Jour. Am. Med. Assn., 1914, **63**, 1456.

[3] Longcope: Factors in the Diagnosis and Treatment of Syphilitic Aortitis, Cleveland Med. Jour., 1914, **13**, 141. Also Syphilitic Aortitis, Its Diagnosis and Treatment, Arch. Int. Med., 1913, **11**, 15.

[4] White, P.: Prognosis in Heart Disease Am. Jour. Med. Sci., 1919, **157**, 5.

[5] Lewis, Sir T.: Clinical Disorders of the Heart Beat, New York, 1918, p. **111**.

THE PROGNOSIS OF ANGINA PECTORIS.*

By Louis Hamman, M.D.,
BALTIMORE, MD.

Before I speak of the prognosis of angina pectoris it is necessary that I define clearly what I mean by angina pectoris. This is necessary because the term is used by physicians and medical authors in a different and almost contrary sense. Some employ it to designate a definite disease with peculiar clinical symptoms and characteristic anatomical lesions, while others employ it to designate a symptom that may occur in many different diseases and therefore without precise clinical or pathological implication. It is obvious that the prognosis of angina pectoris will vary widely with the definition adopted.

The name angina pectoris was introduced by Heberden. What he meant by the term is clearly stated in his classical description. "There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it. The seat of it and sense of strangling and anxiety with which it is attended may make it not improperly be called angina pectoris. Those who are afflicted with it are seized while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their life away it if were to increase or to continue; the moment they stand still all this uneasiness vanishes. In all other respects the patients are at the beginning of this disorder perfectly well, and, in particular, have no shortness of breath, from which it is totally different."

By the contemporaries and immediate followers of Heberden, angina pectoris was used to denote the clinical picture he describes so well. It was only later that the clearness of the picture was blurred by the addition of spurious and irrelevant details. Conditions resembling angina, though but vaguely and remotely, came to be mistaken for it and finally distinctions were so far wiped out that almost every distress and oppression about the heart was called angina. To bring some order out of this confusion Forbes unhappily coined the term angina notha, spurious or false angina. This counterfeit angina was then subdivided into numerous groups, hysterical angina, toxic angina, vasomotor angina, and so on, until medical authors began to describe under the heading angina pectoris such a preplexing medley of symptoms that the original clear sense of the term was totally obscured. Confusion reached its high point in Germany fostered and encouraged by the great clinician Nothnagel. It was commonly stated that at least one-half the cases of angina were innocent functional disorders and that there was no

* Read before the American Climatological and Clinical Association, May, 1924.

sure way to tell the true from the false unless death arrived to give the distinctive stamp. In the latter part of the last century, Huchard fought valiantly to rescue angina pectoris from the perversions that had nearly robbed it of character and individuality. During the past twenty years, English authors, notably Mackenzie and Allbutt, have striven to revive the early definition of Heberden and to restrict the use of the term angina pectoris to the disease he so clearly and distinctly describes. With this reasonable and desirable endeavor I am entirely in sympathy and I shall use the term angina pectoris to denote a definite disease with a definite pathological anatomy.

It is scarcely necessary to plead justification for this choice. I am not here to describe the characteristic marks of the disease angina pectoris; I wish merely to state what every physician of experience knows, namely, that these marks are easily recognized. The diagnosis of angina pectoris is not more difficult than the diagnosis of any other clearly defined disease. Indeed I should say that for the most part it is less difficult. It is true that mistaken diagnoses are sometimes made and that occasionally the most experienced physician will waver in doubt. However, error and indecision are equally frequent in the diagnosis of tuberculosis, typhoid fever, cancer and every other well known disease. The perplexities of the diagnostic problem are no satisfactoy excuse for vagueness in definition. If a disease is diagnosed typhoid fever and autopsy reveals it to have been miliary tuberculosis, we do not speak of miliary tuberculosis as pseudo or false typhoid fever. We humbly admit the insufficiency of diagnostic criteria and the fallibility of medical inference. And so in angina there is no warrant, simply because the diagnosis is occasionally difficult, to further perplex and confuse by claiming relationship where none exists and ignoring differences that are patent. It is time that angina pectoris be accepted at its face value and all spurious, false and pseudo anginas be abolished.

I have said that angina pectoris has a definite pathological basis. Jenner was the first to point to the relation between angina and disease of the coronary arteries. You will recall his anxiety over Hunter's symptoms and his grave suspicions which were fully verified at autopsy. Interest in the anatomical features of the disease was almost lost during the period of clinical confusion when angina meant anything from an instantly fatal disease to a flurry of nerves. Huchard revived the interest when he sought to place the disease again upon a firm clinical basis. The opening sentence of the chapters upon angina in his classical Traité clinique des Maladies du Cœur reads as follows: "The anatomical cause of angina pectoris is a lesion of the aorta situated near the orifices of the coronary arteries, or a lesion of the coronaries with or without aortitis, resulting in a narrowing of their caliber, a diminution or an obliteration of their lumen." To justify his view Huchard collected the records of 185 cases of angina that had come to autopsy and all of them

reported disease of the coronary arteries or of the aorta in the neighborhood of the coronary mouths. Another eminent physician, Allbutt, has more recently considered the matter in detail and comes to a somewhat different conclusion. Allbutt thinks the characteristic lesion of angina is disease at the root of the aorta. He contends that autopsy always reveals this lesion whereas the coronary arteries are often unimpaired. Although the vast array of observation and argument that Allbutt musters to support his view forces us to admit that aortitis at the root of the aorta is often the cause of angina, still the evidence that coronary disease is also frequently the cause is convincing to many. The characteristic symptoms of sudden occlusion of a branch of the coronary arteries and the great frequency of coronary thrombosis as the cause of death, are weighty arguments in favor of the view. While we must wait for fuller knowledge to decide what part is played by coronary disease in liberating attacks of angina there can be no question that the condition of these vessels is the most important single factor to determine the outcome of the disease.

Perhaps I have tarried unnecessarily long to make clear what I understand by angina pectoris even though the question has been but hastily touched upon. The course of the disease as we observe it clinically is so devious and uncertain that we cannot chart accustomed or predetermined paths. Still it will be helpful to draw a number of arbitrary divisions to facilitate description. The disease may manifest itself:

1. By sudden death in the first seizure.
2. By sudden death or death from myocardial insufficiency, after months or years of attacks.
3. By a period of attacks, followed by a long or short period of remission, then a recurrence of attacks perhaps with sudden death.
4. By a period of attacks, followed by a long period of remission during which the patient dies from some other cause. These instances are spoken of as cures.
5. By an unusually severe seizure followed by death, not sudden, but after hours or days of agony, from a gradually failing heart. The seizure may be initial or as is more often the case, follow months or years of less severe attacks.
6. By an unusually severe but not fatal seizure followed by a period of apparent recovery and months or years later by sudden death from rupture of the heart or gradual death due to advancing myocardial insufficiency.

We are then confronted by a disease which may strike with instant death in the midst of seeming health and yet from which an afflicted man may apparently recover and live on for many contented and useful years. Since any course is possible between these contrary extremes prognosis is indeed difficult and uncertain. If we were able to see clearly into the fundamental differences that distinguish

the abruptly fatal from the curable instances of the disease, prognosis would then be upon a firm basis. At the present state of our experience we are able to make only uncertain conjectures. However, a number of interesting considerations are at once suggested. Sudden death in angina is usually associated with occlusion of a branch of the coronary artery. In these instances the mechanism of the fatal issue is theoretically clear. With the sudden plugging of the vessel a large area of ventricular muscle is deprived of its blood-flow and the functional changes that must promptly follow lead to ventricular fibrillation and immediate death. There is much suggestive evidence from animal experiments and from the observation of human cases to support this view. When a coronary vessel is tied off in a certain number of instances extrasystoles develop, then paroxysms of ventricular tachycardia, then ventricular fibrillation and death. The same sequence of events has been observed in man following coronary occlusion. It is true that in animals as a rule death does not occur immediately upon ligation of a coronary artery, but when death does occur it seems always to be due to ventricular fibrillation. Instances are reported of sudden death in angina in which it is stated that at autopsy the coronary arteries and heart showed no abnormality. If we accept these data as conclusive we can give no satisfactory explanation of the mode of death. Allbutt argues in detail for a vagal inhibitory death. However, there is no experimental evidence to support the adequacy of such a mechanism.

Since angina may be due to changes at the base of the aorta as well as to disease of the coronary arteries, it seems reasonable to assume that attacks associated with coronary disease will have an ominous outlook, whereas attacks due to small sclerotic patches in the aorta will have a relatively favorable prognosis. As in other functional disturbances there is here apparently no correspondence between the extent of the pathological change and the degree of functional disorder. A small lesion may produce severe symptoms whereas extensive and sometimes extreme changes may be present in the absence of any symptoms whatsoever. There are reasons for these variations but our knowledge is too meager to elucidate them. I see no satisfactory way to explain long periods of remission, apparent cures, or the duration of recurring attacks over decades without assuming that relatively small lesions may liberate disproportionately severe symptoms. If we were able to gauge by clinical methods the seat and extent of the lesion we would be upon safe ground for prognosis. It is needless to say that we are unable to approach this desired position. We may only view it from a remote distance.

There are two common causes of aortic lesions associated with attacks of angina pectoris, infections and arteriosclerosis. Among the infections syphilis predominates. It is said that angina may follow attacks of influenza presumably due to mild aortitis which may subside. Such cases are reported but as far as I know none are

verified by postmortem examination. Many of them recover as might be anticipated if the anatomical conception is correct. Similar instances are said to follow rheumatic fever. Syphilitic aortitis is the disease above all others which produces lesions at the very base of the aorta, the location which Allbutt believes is especially concerned in the initiation of attacks of angina pectoris. As is well known the favorite site of arteriosclerotic lesions is higher up in the aortic arch. Syphilitic aortitis frequently narrows or occludes the mouths of the coronary arteries, but it rarely invades the coronaries themselves. However, in spite of this favorable location, syphilitic aortitis is relatively seldom accompanied by attacks of angina pectoris. Paroxysms of oppression with suffocation are common but these are not genuine angina. Arteriosclerotic lesions are frequently associated with sclerosis in the coronary system. Symptoms associated with arteriosclerosis occur as a rule later in life than the symptoms of syphilitic aortitis. These facts offer a satisfactory explanation for certain clinical relations of angina pectoris.

Angina occuring between thirty-five and forty-five years of age is usually due to luetic aortitis. If luetic aortitis can be excluded then the chances are in favor of coronary artery disease. In certain families a remarkable number of the males die of angina between forty and fifty years of age. In either instance the outlook is unfavorable for permanent relief from the attacks or for many years of life. Angina coming on after fifty years is usually associated with arteriosclerotic lesions. It is impossible to predict the state of the coronary arteries. However, I have the impression that cases of angina associated with moderate hypertension, with evidence of sclerosis of the aorta as indicated chiefly by the characteristic bell-like quality of the second aortic sound and perhaps with slight enlargement of the heart, are more likely to run a mild and prolonged course than are those with normal blood-pressure and normal heart sounds. Clinicians, as a rule, fear angina when examination of the heart reveals no abnormality.

In addition to attempts to fix the location of the anatomical lesion we may try to gauge its extent by functional studies. As I have said prognosis depends chiefly upon the condition of the coronary circulation and we may get some estimate of its capacity by careful inquiry into the reserve power and the recuperative ability of the heart. When attacks of angina follow slight exertion or occur when the patient is at rest the outlook for improvement is not so good as when they come only upon vigorous exercise after meals. Again, if a judicious regulation of the patient's life is followed by a cessation of attacks or a marked diminution in their frequency and severity, the forecast is better than it would be if no such obvious benefit should follow the regulation. Yet again, the response to a period of complete rest in bed is an important indication of the gravity of

the underlying process. In a word, when angina comes on in the midst of a busy, active life and the symptoms subside or greatly improve following rest or the curbing of pernicious habits, then the prognosis is good, within the limits set by the nature of the disease; on the other hand, when angina comes on with but slight provocation and persists unabated by judicious care, then the prognosis is ominous. These dicta are too terse to contain the whole truth and many flagrant exceptions may be noted. They are deductions that fit reasonably well to large groups of cases but may ill become the isolated case. Months of careful observation may be necessary to reach a satisfactory conclusion about the response of the heart to rest, exercise, worry, care, infection and the many other influences that may act upon it beneficially or harmfully. But this time is not lost nor wasted; for the guiding principle of treatment is to restrain the patient within the bounds of his functional range, and to treat him well imposes the obligation to study the functional range with all possible care.

Important help in prognosis may come from electrocardiographic studies. Certain alterations in the *QRS* complex and in the form and direction of the *T* wave are interpreted to indicate diffuse myocardial damage. Smith has shown that when in dogs large branches of the coronary arteries are ligated the amplitude of the *QRS* complex is diminished and the limbs are often notched. At the same time the *T* wave is inverted in one or more leads, is increased in size and may arise from the descendant limb of the *QRS* complex before the isolectric point is reached. Similar curves have been recorded in man after coronary occlusion. When these electrocardiographic changes are observed in patients with angina pectoris they suggest serious myocardial damage and are therefore of grave significance. However, they cannot be interpreted in a uniform way. The changes are often transient and they may be entirely absent in patients who die soon after in an attack. Inversion of the *T* wave has been regarded as a particularly ominous sign.

Angina is always a serious disease and the outcome is uncertain. Sudden death occurs so frequently that it is looked upon with terror by the laity and with trepidation by the profession. It is but natural that this dramatic and awe-inspiring event should dominate the emotional reaction toward the disease and color it with fear. However, if the situation be regarded with calm deliberation it is not so fearful as it appears. In contrast to this tragic ending a number of palliative and reassuring facts emerge. The disease is commonly of long duration and with proper care periods of remission are the rule. These periods of remission may be so indefinitely prolonged as to simulate a cure. Every older physician will readily call to mind patients still living in active comfort about whose future he may have entertained the gravest fear ten years ago or

longer. It is both just and wise to stress this benign and favorable aspect of the disease and to hold it ever before the mind as a corrective to the overpowering emphasis of sudden death.

Sudden death in the first seizure of angina is a rare event. Perhaps it is rarer than it appears to be. I think it is because in instances of severe attacks, seemingly initial, from which patients recover, they nearly always give a clear history of preceding attacks which went unrecognized. A year ago I saw an unusually vigorous man of sixty-seven years whose youthful activity was generally remarked upon. In the midst of apparently robust health he had a terrific attack of angina due to occlusion of a branch of the coronary artery. In the light of this event attacks of so-called indigestion which he had had for five or six years preceding won a new and sinister significance. Without a suspicion of their true meaning he described graphically attacks of gas with pain under the sternum that momentarily stopped him short in the midst of exertion. I recall two of my associates carried off suddenly in the heat of a busy practice. The intimate friends of each knew of preceding warnings, warnings that did not go unrecognized by the victims.

Sudden death after months or years of attacks is not uncommon. Patients often accomplish an unbelievable amount of work in spite of ever recurring attacks. John Hunter lived for twenty years, and did much of his best work while subject to attacks. I recall a very intelligent professional man I saw on several occasions some years ago. He had severe attacks of angina and fully appreciated the gravity of his symptoms. The attacks were so frequent and alarming that his courage and endurance were undermined and he lived miserably in constant fear and apprehension. I chanced some months later to meet him casually upon the street and I was amazed at the change in his appearance and bearing. He walked briskly with firm step and head erect, the unconcerned smile of healthy vigor and confidence upon his face. He greeted me cordially and yet passed by so quickly that I could not mistake his desire to avoid further intercourse. I spoke of the change to his physician and congratulated him upon the obvious marks of his therapeutic skill. He replied that he as well as all the friends of the patient had noticed the change and commented gratefully upon it but that he could not take any credit to himself since the patient had passed from under his care. He went on to explain that the patient had embraced Christian Science and become an ardent disciple of that cult. Fortified by these strange but powerful convictions he went daily to his work and it is not hard to imagine the storms he encountered unflinchingly and without complaint. Some time later, at noon one day he left his office to go to lunch and dropped dead upon the street, as was reported, in an attack of acute indigestion. I still see from time to time a man now aged sixty-seven years who consulted me in 1916. His first attack

of angina had come on a few weeks before while running for a car and since then attacks had recurred on exertion. The physical examination was negative except for enlargement of the prostate gland. The urine contained small amounts or sugar which disappeared upon a moderate regulation of the diet. In 1918 the urinary difficulty became urgent and it was necessary to introduce temporarily a retention catheter. A year later increasing difficulty of urination forced the serious consideration of operation. Constantly recurring attacks of angina led to frequent postponement until finally the operation was successfully performed. The patient made a good recovery and has been better since although he continues to have angina when he overexerts. He is a man of large business interests and he leads a very active life.

Long periods of remission, even after severe attacks, occur frequently. One is never justified in saying that patients with angina are cured, because even though symptoms are absent the underlying anatomical lesion remains. In most instances, if the patient lives long enough, the attacks do recur. In March, 1921, I saw a lawyer, aged sixty-two years, who was having very characteristic and severe attacks of angina. He told an interesting story. In 1913 he was appointed police magistrate and was obliged to work very hard under a good deal of nervous pressure. He had always been interested in sports and had previously taken much out-door exercise, but his newly-won position necessitated abandoning this life-long habit and leading a sedentary life. He gained weight rapidly and soon began to have severe attacks of angina. His blood-pressure was taken and he was told it was very high. When the patient left the bench and again took up exercise his weight fell off and the attacks of angina disappeared. After about four years of good health the attacks came back but were not so severe as they had been before. At the time I examined him he had been having attacks at short intervals over a period of eighteen months. He refused to accommodate his habits in the slightest way to his symptoms and insisted against all advice in pursuing his accustomed activities. Two weeks later he had an appalling attack of angina due no doubt to occlusion of a branch of the coronary artery. He did not rally from this attack and died about forty-eight hours later.

Severe attacks of angina followed after a few hours or a few days by death or by recovery to end months or years later from myocardial insufficiency or rupture of the heart, are characteristic of occlusion of a branch of the coronary artery. It is only within the past fifteen years that a precise clinical picture of coronary occlusion has been drawn. Obrastzow and Straschesko in 1909 were able to find only 3 instances in which the diagnosis had been correctly made. American clinicians have added valuable contributions to the subject and the diagnosis is now relatively easy. However, the great variation in symptoms is astonishing. A number of

instances are reported in which one of the main branches of the coronary artery was found at autopsy to be occluded, although no evidence of cardiac disease had been discovered during life. There is a liberal anastomosis of the coronary arteries between the small branches of its different divisions and also with branches from contiguous vessels supplying the pericardium and the epicardial fat. If a large branch of the coronary artery is slowly occluded and sufficient time is given to allow the development of an adequate collateral circulation, the final closure of the vessel may go unmarked by any symptom. Gross has published such an instance and his beautiful photographs show an astonishing development of the rami telæ adiposæ. On the other hand if the occlusion comes suddenly the accident may be marked by the most dramatic and agonizing clinical manifestations. The severity of the shock may be estimated by the conspicuous fall of blood-pressure which nearly always accompanies it. In 1 patient following an unusually severe seizure there was anuria for over twenty-four hours. Blood-pressure observations were not made during this period but the pressure must have fallen temporarily to a point so low that the secretion of urine was interrupted. And yet, although for a week the patient wavered upon the threshold of death, he finally recovered and a year later is quite well except for some breathlessness on exertion. As observations multiply it becomes more and more apparent that death by no means always follows the accident. Indeed it appears that more instances recover than immediately succumb. In 1918 I saw a patient who three years before had had a severe attack of angina from which he recovered. He then remained well and free from attacks until twenty-four hours before my visit. While at the theater he was seized with a violent paroxysm of pain followed thirty-six hours later by pulmonary embolism. The patient was desperately ill but recovered and remained well for four years when he had the third attack which was fatal. Similar observations are being rapidly multiplied and as diagnosis improves I think we will be more and more surprised at the large number of recoveries following coronary occlusion.

Conclusion. I should like to summarize briefly the impressions I desire my remarks to leave behind them. Although angina is a serious disease often accompanied by sudden death, still it is compatible with many years of useful life and often is characterized by long periods of remission which sometimes resemble cure. We have no sure way to distinguish the malign rapidly fatal cases from the benign ones which last for a decade and longer. However, a careful consideration of the nature of the underlying process and a study of the functional range of the heart will give us valuable data upon which to risk a forecast. At present prognosis is in the stage of group prediction. As information grows we may be able to see more acutely into the differences and predict with some degree of probability the course of the disease in the individual patient.

PROGNOSIS OF THE TACHYCARDIAS.*

By James S. McLester, M.D.,
BIRMINGHAM, ALA.

The fate of the man with heart disease depends upon the integrity of his myocardium. This is just as true of those abnormal states which are accompanied by tachycardia as it is of all other forms of heart disease. Tachycardia is a mere symptom, and the prognosis depends upon the underlying disease, in last analysis upon the influence of this disease upon the heart muscle.

From an etiological standpoint rapid heart action is of three types: (1) That of purely nervous origin; (2) that which accompanies lowered myocardial efficiency, and (3) that which follows a change in the location of the pace maker.

In the first group, the tachycardias of purely nervous origin, there is no genuine cardiac disease, and the fate of the patient has little to do with his heart. Here should be included the effort syndrome. Just what factors are back of this interesting symptom-complex, whether nervous or otherwise, it is difficult to say, but we are justified in assuming that the patient's disability rests not upon lowered cardiac efficiency but rather upon the factors underlying his abnormal psychic state. It is his ability to cope with the latter which determines his fate. We can therefore dismiss from present consideration the effort syndrome and the other tachycardias of nervous origin.

In the second group, the tachycardias due directly to loss of myocardial efficiency, there are included many diseases of widely varying pathology and of all grades of severity. At one end of this group, among the diseases of less serious nature, stand those which produce so-called palpitation. In spite of its lack of seriousness it should not be forgotten that palpitation always means increased myocardial excitability, which in turn indicates some form of myocardial injury; an infection or, if you please, an intoxication.

True palpitation can be distinguished from the purely neurotic states by the short, quick contractions and accelerated conduction time. The pulse-rate rarely exceeds 150; its onset is gradual; likewise the return to normal is gradual; and it is profoundly influenced by rest. These last characteristics serve to definitely distinguish palpitation from the rapid heart action of paroxysmal tachycardia.

The prognosis in cardiac palpitation depends upon the nature of the intoxication (or infection) and upon the degree of damage done the myocardium. For example, while the palpitation seen

* Read in a symposium on prognosis in heart disease at the meeting of the American Climatological and Clinical Association, Atlantic City, May 2, 1924.

during or shortly after many infectious diseases, such for instance as pneumonia or typhoid fever, bodes little or no ill, that which accompanies certain other infections such as rheumatism is of more serious moment. Rheumatism not infrequently produces a myocardial injury which is progressive in nature and therefore of grave significance. On the other hand, when the poisoning is not of bacterial origin, such as occurs in chronic alcoholism, a cessation of the intoxication will lead usually to a gradual restoration of myocardial efficiency.

Belonging in this group is the tachycardia of exophthalmic goiter. This is an expression of the poisoning to which the myocardium is subjected. The outlook depends upon our ability to stop the process, and therefore in last analysis upon the behavior of the thyroid gland.

Another type of tachycardia is that exhibited in fibrous or fatty degeneration of the myocardium. Here the outlook is determined first by our ability to find the cause and to halt the progress of the disease, and second by the functional capacity of the remaining myocardium.

Rapid heart action is also encountered in patients with valvular cardiac disease. We should not judge, however, of the extent of myocardial strain to which these patients are subjected merely by the increase in pulse-rate which follows exertion: this may be misleading. Of more importance is a sustained rapid rate which persists even during rest, for this always indicates extremity of cardiac effort.

Often a quick pulse is the first evidence of some debilitating disease such as pernicious anemia or cancer and the prognosis is correspondingly grave. On the other hand, it should not be forgotten that a great many people live normal lives and show no signs of trouble, although there is at all times an increased heart-rate. Therefore, tachycardia alone cannot be taken as evidence of disease; the patient must be studied as a whole.

For the more accurate measurement of the cardiac efficiency of the patients of this group, numerous methods of precision have been devised, but none of these are entirely satisfactory. There is no easy way, and we must resort always to painstaking clinical observation. Of greatest prognostic importance, no matter what the cause of the tachycardia, is the degree of discomfort and distress which the patient experiences after exertion. To observe closely the manner in which the patient as a whole reacts to physical effort; to watch for signs of early exhaustion, such as dyspnea on slight exertion; and to discern other signs of myocardial weakness such as slight edema; these are the only means of detecting impending cardiac failure.

The third group of tachycardias, those in which the abnormal rate comes from abnormal origin of impulse, presents on the whole

a still graver prognosis. This group includes auricular fibrillation, auricular flutter and paroxysmal tachycardia.

Auricular fibrillation could with equal propriety be placed in either this or the previous group, for while it is dependent upon a definite change in the location from which come the cardiac impulses, it represents also myocardial disease of the gravest type. It indicates that severe strain has been thrown upon a diseased myocardium and that the heart is "in extremis."

It is sometimes of prognostic value to know how the patient deported himself before the onset of fibrillation. If he was easily exhausted and early showed other signs of cardiac failure, then fibrillation by adding to the burden of an already over-taxed heart, increases greatly the gravity of the prognosis.

The outlook, at best, in this type of disordered and irregular ventricular action is always grave, but the degree of gravity depends in part upon the nature of the disease which is responsible for the myocardial breakdown; whether for instance, it is rheumatic, renal or arteriosclerotic. If in addition to the disordered rhythm there is a continued high ventricular rate, even after rest and judicious medication, then we are justified in assuming that disaster is imminent.

The extremity of the patient's distress, his reaction to effort, and his response to treatment, as well as the signs immediately referable to the heart, such as liver engorgement and edema, offer the best criteria upon which to formulate a prognosis. The fact always remains, however, that auricular fibrillation in the vast majority of instances heralds oncoming failure and an early death.

Akin to auricular fibrillation is auricular flutter. While this condition is sometimes difficult to distinguish from paroxysmal tachycardia, the fact that it occurs in elderly individuals with arteriosclerosis and other evidences of cardiac disease, suggests a kinship to fibrillation rather than paroxysmal tachycardia. In distinguishing auricular flutter from paroxysmal tachycardia an arbitrary pulse-rate, 200 per minute, is taken as the dividing line; a ventricular rate above 200 is believed to indicate the former, while a rate below this indicates the latter. It is only by means of an electrocardiograph, however, that we can with assurance recognize auricular flutter.

The prognosis in auricular flutter, as in other manifestations of myocardial impairment, depends upon the nature of the underlying disease. Its gravity is also indicated by the ease with which the patient responds to effort, and particularly by his reaction to treatment. When, as the result of treatment, the flutter ceases, there is always an immediate improvement in his general condition. If flutter can thus be controlled by treatment the prognosis is relatively good, but if rest and appropriate medication do not terminate the flutter, then the outlook becomes extremely grave.

Paroxysmal tachycardia is accompanied by two dangers. First, the patient may die during the attack. This, fortunately, is extremely rare, and the individual attacks taken alone are usually not of great danger. Second, the attacks may become so frequent and of such long duration that they finally exhaust the heart muscle and lead to death from myocardial failure. Since no one can offer a prediction concerning this first factor, sudden death during the attack, it is the second factor, the exhaustion of the cardiac muscle, which interests us. Attacks of paroxysmal tachycardia may recur through a great many years, even decades, without serious consequence. I now have in my care a woman who has had frequent attacks of this disordered heart action for forty years, and it is only within the last few months that the heart has shown signs of failure.

The prognosis in continued attacks of paroxysmal tachycardia is in turn determined by two factors: First, the endurance of the heart muscle, and second, the severity of the strain which the heart must bear. As in other forms of heart disease, we judge of this first factor, myocardial integrity, by nothing the reaction of the patient to the paroxysms. If during the attack there are signs of myocardial failure, such as cardiac dilatation, great exhaustion, and pulmonary edema with cough, the prognosis is bad. And if to this there are added signs of cardiac weakness, between the paroxysms, then the outlook becomes especially bad. If, on the other hand, the patient stands the attacks well, and if between attacks he is able to withstand fatigue and can without too great effort undertake the work of the average individual, the prognosis is good.

When the patient is seen for the first time, something can be predicated upon the length and frequency of the paroxysms of the past and his subjective reaction to these attacks. If the attacks are increasing in frequency and severity, and if there are already present signs of beginning cardiac failure, then the outlook is bad. The patient with forty years of paroxysmal tachycardia whom I have just mentioned, is now having paroxysms of ever increasing severity and of longer duration. These attacks are now accompanied by cough and occasional edema of the lungs, and the prostration of each is profound. It would appear, therefore, that unless the quinidin, which we are now using, fulfills its promise and controls the attacks, the end is near.

Conclusion. The prognosis in the various tachycardias should be based on two factors: First, an understanding of the pathological process which causes the abnormal rate; and second, upon accurate clinical observation concerning the ease or difficulty with which the patient meets the handicap imposed by the disease.

TUMORS OF THE BREAST: A CLINICAL CONSIDERATION.*

By John F. Erdmann, M.D.,
NEW YORK.

In correlating material for this paper I have collected from my card index all operations upon the breast except those for mastitis, either chronic or suppurative, during the period from January 11, 1905, to and including August 15, 1923, about eighteen years, and find recorded in the index 539 cases. There were also in this series 22 carcinoma recurrence operations, which were in part mine and the remainder patients of others, one of these being operated upon four times in the scar and remote areas. Of the operated cases 315 were carcinoma, 1 of the entire number being a well-advanced bilateral manifestation. There were 141 cystadenoma, of which about 117 were unilateral and 24 bilateral; sarcoma, 2; tuberculosis, 2; lipoma, 4; aberrant breast, axillary, 3, 1 of which was carcinomatous, 1 sebaceous cyst of good size, 1 hemorrhagic cystadenoma; adenofibromata and fibrocystadenoma, 27; peri- and intracanalicular fibroma, 38, of these latter in all 65 (including intracanalicular cystadenoma and intracanalicular papilloma, etc.).

It will be observed in the figures that about 60 per cent of all the cases selected for operation were carcinoma. These operated cases do not represent by far the patients seen with cystadenomatous degeneration of such slight degrees as to be considered non-operative. Neither does the large number of cystadenomatous breasts operated upon represent an evidence of operative furor in this class of pathology, but they were in all instances patients with this type of degeneration so far advanced as to demand operative relief. Numbers of them had had single cyst operations done on various occasions, one in particularly asking for radical relief after five individual operations had been done by various operators, each operation being guaranteed as being the last of her trouble.

It has been my experience to see but 2 tuberculous tumors and 2 sarcomata in this period of time and 1 aberrant breast undergoing malignancy, which finally required a reoperation, including the previously normal breast.

There are 4 instances in the carcinomata in which the second breast was invaded. One of these patients was inflicted with the second growth so remotely placed from the chain of lymphatics as to lead me to consider the tumor of primary origin, equal to that of the first breast. There was 1 bilateral carcinomatous involvement almost equal in both breasts. The case is so interesting as to deserve recording.

* Read before the Springfield, Mass., Academy of Medicine, December 11, 1923.

CASE HISTORY.—C. M., aged forty-seven years, single, was admitted to the New York Post-Graduate Hospital, March 17, 1921; discharged, March 28, 1921.

Chief Complaint. Tumors of the breast, duration seven months.

Family History. This was negative, as was the past history. There were no operations and no previous illness of moment.

Personal History. The menopause occurred two years ago, with some slight spotting since.

Present Illness. Began seven months ago, without pain and with no discharge from nipple. There was no loss in weight.

Surgical Condition. There is a definite assymetry of the two breasts. The left presents a flattened-out and retracted nipple. The entire breast is hard, rubber-like in consistency. It moves as a whole on the chest. There is a large hard gland in the axilla, freely movable and smooth. The right breast is very hard, especially about the nipple. There is no retraction of the nipple, but the skin retracted in other areas and very adherent to the underlying tissues. There are a few very small hard nodes in the axilla.

Operation. Bilateral Stewart incision; result: primary union.

Pathological Report. Bilateral scirrhous carcinoma, with metastasis to lymph glands.

The pericanalicular and intracanalicular tumors were seen in the female, usually from seventeen to thirty-five years of age. The cystopapillomata, of which quite a few were recorded, were easily diagnosed at the first visit by the characteristic discharge from the nipple. In the non-recorded cases of mastitis, I am quite satisfied that 3 recently operated upon were fat necrosis cases of the type described by Burton Lee. In neither of these did I remove more than the areas involved.

As to the question of bilateral involvement being primary or of the second breast being invaded through lymphatic conveyance, one is unable to decide, but I am rather fixed in my opinion as to 2 of the patients specially cited. In the instance of the patient with the immediate bilateral involvements I am inclined to believe after very careful examination and cross-examination that the breasts were simultaneously invaded by primary growths, or almost so; at least I feel that neither growth was a metastasis from the other.

In a patient with involvement of the remaining breast four years after the removal of the absent breast, the zone occupied, the discrete type of tumor, absence of any infiltrating process from the removed side and the absence of evidence by roentgen-ray of any other metastases, lead me to a positive conclusion that involvement of the remaining breast was as much of a primary growth as the tumor in the removed breast. Unless we can definitely trace the metastatic chain across the breast, such instances as the one just cited should be classed as primary and not as metastatic.

In this series of patients but 3 were in the male, 1 a recurrence and 2 primaries. I have previously reported[1] on 3 male patients with tumors of the breast.

Diagnosis of Malignancy. The most frequent reason, barring the presence of a tumor, that patients advance for suspecting malignancy is pain. It is most gratifying to be able to tell these worried callers that malignancies of the breast never begin with pain, that when pain is a symptom of cancer it requires no expert to diagnose the condition and that the pain in these patients is due to compression involvement of the nerve filaments, infiltration, or a large tumor, or exposed nerve filaments in an ulcerating tumor. As a rule, malignancy of the breast is a single tumor, as compared with multiple tumors in cystadenoma or fibroma, although one occasionally sees a malignancy present with a well-defined multitumor not of the cystic variety. Recently I have removed a carcinomatous breast with two distinct nodules, 4 inches apart. The bilateral breast tumors are most frequently the cystadenomata and fibromata.

No better diagnostic objective evidence is known than the dimpling of the skin when the breast is grasped, as compared with the full rounded convexity of the normal breast when compressed between the examining fingers. This dimpling sign of malignancy is obtained very early. By lifting the breast from below, or by compressing it between two or more fingers, the dimpling will readily follow, while in the non-involved breast the convexity will remain or be exaggerated. This dimpling can also be seen without difficulty either by direct or by oblique inspection, and by feeling carefully over the dimple one obtains with the palpating hand the sense of hardening or tumor. In patients with more advanced, or in patients with a more disseminated growth, the classical orange-peel skin is seen. The elevation of the breast affected above the plane of the other, due to the lifting effect of the involved tissues, is seen in more advanced conditions. Strongly abducting the arm from the side, thereby making the skin and pectoralis major tense, will often bring the tumor into bold relief. Compression of the breast upon the chest wall, with the patient prone or in erect posture, is an excellent means for detecting irregularities of the breast.

Retraction of the Nipple. If one were to rely upon this condition for a diagnosis operations upon the breast would be more common than those for the appendix. In a very large proportion of patients there are single or bilateral retracted nipples in breasts that are absolutely normal otherwise. The retracted nipple of malignancy is due to the same cause as the dimpling of the skin mentioned above. Eversion of this latter type of retraction is usually impossible, while in the normally retracted nipple eversion is quite possible in the great majority.

[1] Dennis: System of Surgery, 1896, **4**, 944.

Axillary Adenopathy. To be found readily on palpation in the majority of patients, it requires an exceptionally enlarged gland, or an exceptionally thin subject is essential.

Metastases. These are important in their bearing upon the question of operative justifiability. One cannot be too careful in the readily palpable tumor in the search for secondaries, those of the mediastinum or lungs, characterized by a dry cough; in the bones by pain allied to nerve distribution pains, such as facial, intercostal and, in my experience, frequently in the course of the sciatics, one or both.

One of my patients lived eleven years after a very extensive dissection. The first evidence of metastasis was a hoarseness of voice, increasing slowly in intensity. It was not suspected that the hoarseness was in any way due to metastasis from the growth removed almost eleven years before until roentgen-ray showed a tumor, the shadow of which was the size of a tangerine and situated above the arch of the aorta.

As far as my personal observations go, I cannot encourage the idea that metastases occur in the abdominal viscera in such frequency as we are lead to believe by various observers. Therefore, I am not inclined, in all patients, to practise Handly's resection of the upper segment of the rectus fascia, although I frequently do it.

In addition to the remote sites mentioned, the immediate sites call for consideration. Recurrence in the scar can be assigned to too small a skin-flap removal; implantation by the using of forceps in the flap edges that have not been properly cleaned after use in the ablated portion; the conveying of cells on the gloves, towels, sponges and other instruments, that have been in contact with the removed area. The fact that cells may be lodged in the lymphatic channels at a remote area must account for those shot-like bodies seen later at a distance from the scar of operation. Occasionally the shot-like masses in the area formerly occupied by the breast are cystic formations about a ligature, and will disappear in time.

No breast should be removed when the supraclavicular and cervical glands are so metastatically enlarged as to be readily palpated, but should be subjected to roentgen-ray or radium for a time. This same statement holds in those patients with massive skin infiltration. I have recently had a marvelous disappearance of the skin infiltration in a woman, aged thirty-eight years, after roentgen-ray application by the more recent high voltage machine, although the tumor proper maintained its original size after six months' treatment. This patient was subsequently operated upon and died in six months, even with added postoperative roentgen-ray exposures. No breast should be operated upon with a promise of cure or a great extension of life in which the growth, ulcerated or not, is adherent to the chest wall. This type should also be sub-

jected to radiotherapy, exceptions being in the instances when one can remove the ulcerating tumor and cover either by plastic or by grafting processes.

I believe that tumors, when they are small, should be operated upon, and not treated by roentgen-ray until after operation. A regrettable incident occurred in my practice in 1921. A patient with a small nodule in the upper inner quadrant of the right breast was advised by me to be operated upon. However, she had a relative connected with a large hospital, which deals largely with malignancies, and is well furnished with radium and roentgen-ray appliances. By this overenthusiastic relative, the patient was given every confidence of cure, and I lost sight of her for six months. Upon her return to me at the end of this period, during which, she stated, she had been told that she was cured, the growth was still present, decidedly larger and, in addition, there was distinctly evident adenopathy. Operation was again advised and consent at this time given. The removed growth was carefully examined by a pathologist, and no cell changes, due to roentgen-ray "sickening" or destruction, was observed by him.

Recurrences may be exceptionally rapid, and again very slow. The explanation for either is not ordinarily obtained from the pathologist. At times he will predict rapid recurrence, as was done in the case of the patient with mediastinal growth eleven years after the operation. This patient was considered by two pathologists to be liable to a rapid, six- to twelve-month, recurrence, and without roentgen-ray or radium treatment lived eleven years before showing a suspicion of a secondary tumor. No autopsy was done in this case, so that even with the roentgen-ray picture we are still in doubt as to the nature of the growth. Recently I have been notified of the death by senile dementia of a former patient of mine from whom I removed a breast sixteen years ago. The prognosis made by the pathologist was that of a rapid return. No evidence of a recurrence was observed, however, by her last attending physician. The youth of a patient, as in cancers at any site, is a strong factor in early or rapid recurrence or metastasis. The zone of the tumor, I am led to believe, may also be a factor in rapid metastasis. My most rapid recurrences under this heading are secondary to tumors in the axillary border of the breast, and also in the fat type of patient more frequently than in the lean.

The question of doubt in diagnosis may in most instances be determined by an immediate pathological examination of a frozen section. I do not believe that a wide resection of a growth for immediate analysis endangers the patient at all. I cannot make the same statement for those patients in whom the specimen is removed days or weeks before the breast is removed. The clinical picture on gross section of these questionable growths is, as a rule, so clear that the experienced operator in the majority of instances does not require the microscope except as a confirmatory measure.

Roentgen-ray or radium as a preliminary to operation is, in my opinion at the present time a "follow-the-leader game" that will require some years to satisfy us definitely as to its practicability. Use of these agents subsequent to operation is today largely enhanced by the advertisement the agents have received in the public press and by the friends of the patient. I am at present compelled to say that my cases longest free from metastasis were not treated with roentgen-ray, as at that time roentgen-ray and radium were not in their present-day positions.

To be effective in the prolonging of life or producing a cure, at present the most painstaking and extensive dissections are necessary. I am unfortunate in this discussion in being unable to bring before you statistically my recurrences as to site and time, as but forty-three replies were received to one hundred and fifty questionnaires sent. Neither am I going to entertain the question of pathology. The most radical operation consists in the complete resection of the pectoral muscles, cleaning out of the axilla of glands and fat, and extending the excision at times to the supraclavicular space. I do not demand the removal of the pectoralis minor, except when unable to freely approach the vessels and nerves of the axillary and subclavicular zone. No functional disturbance follows the removal of both pectorals, therefore no hesitancy in removing them should exist.

The questions to be considered in a breast amputation must be: Is it justifiable from the standpoint of recurrence or metastasis? Is the mortality chance sufficiently low? Will the functions of the upper extremity after operation be preserved? The answers to two of the preceding questions are self-evident as a rule.

The functions of the upper extremity should never be involved. Free motion is always possible when orders for motion are properly carried out in practically every incision devised. The greatest impairment of motion may arise in the Willy Meyer-Halsted incision of years ago, where the axillary edge of the pectoralis major is followed. This line of incision when healed has to be stretched when abduction is instituted, and therefore in the nervous and hypersensitive individual limitation may be the result. If, on the other hand, the modified incision be used in which the incision slopes gently over the deltoid with convexity upward, when the arm is abducted the points of origin and termination of the incision are brought together. The Stewart incision has been used in over 85 of my patients since 1916, with no great difficulty in exposure and no great obstruction to motion after the first few weeks, although many patients complain that the upward (abduction) movement drags on the chest wall scar in the early period following operation. The advantage of this incision is purely cosmetic, and should be used in selected cases only.

The mortality in my carcinoma cases was 2, and these deaths

were partly attributable in all probability to a siege of Streptococcus hemolyticus infections that we had in the hospital at that time, also in 1 of these patients due to a second operation being done within eight or nine days subsequent to the first. This patient refused anything but a removal of the suspicious growth and demanded waiting for eight or nine days after being told that the pathological report was carcinoma. On operating radically, the area from which the tumor had been removed was found filled with clot and the surrounding tissues ecchymotic. A complete removal was done, a rapid rise in temperature to 103° F. in two days, purulent metastases were observed all over the body, joints and cellular tissue, with death resulting in ten days. Culture returns from the pus at the various sites was always that of Streptococcus hemolyticus.

It is very pleasing to record relatively few chest complications in so large an area of exposure to trauma and infection in the respiratory zone.

Cystadenoma, single cyst, or the blue-dome cyst of Bloodgood, cystofibroma, multiple cyst, intracanalicular, pericanalicular, or adenofibroma, are, as a rule, readily diagnosed.

In the cystadenomata and multicystic breasts one feels a single or many small nodules. Very often careful massage from the periphery to center will cause to be extruded from this nipple a fluid varying in consistency and in color from watery to pale straw, purulent or milky, bloody or chocolate-brown appearance. In all but the bloody or chocolate-colored fluids one can safely say that he is dealing with a benign condition. This type of growth is also prone to be bilateral. Recently I removed the remaining breasts of 2 women previously operated upon, the one nine years and the other six years, for the same disease. Among its many names, the term "old maid's breast" is frequently applied. When the discharge is bloody or chocolate-colored the diagnosis is usually that of intercanalicular papilloma or a papillomatous cystadenoma. Again, this bloody type of discharge may be due to bleeding from a non-papillomatous cyst with a malignant growth in the wall of the cyst. In the latter instance the precautions taken in a definite malignancy had better be observed. By careful palpation one is often able to outline a tumor in the area circumscribed by the outer margin of the areola and usually close to the nipple. On section of this tumor the eye frequently sees the cockscomb-like papillomatous growth. These processes usually grow from the inner wall of one of the larger ducts. The question of these papillomata being malignant is disputed by many. I believe that a papilloma of the breast is as dangerous as a papilloma of the bladder or rectum, and that, therefore, radical removal is in order, at least the removal of the breast is demanded.

In an article published by me[2] I called attention to this type of tumor, recording a series of 17 patients, with several illustrations taken from the removed breasts, presenting very typical papillomatous growths, and cited the work of A. A. Strasser, Arlington, N. J., who credits Bowlby[3] with being the first to use the term duct papilloma. I further stated that the question of malignancy in the early stages can be answered in the negative, but that they do become malignant, as evidence, Greenough and Simmons report 14 per cent in the pedicles and Bloodgood at that time claimed 50 per cent in the cases observed at the Johns Hopkins. My conclusion in this quoted article was that in small growths excision of the growth suffices, while in larger growths amputation of the breast is imperative. I shall modify this now by saying that I feel that all papillomatous breasts should be amputated.

Intra- and Pericanalicular Fibroma. In 1 instance a very large growth involving the left breast, weighing 5 pounds, was removed, the clinical diagnosis of which was sarcoma, the pathological that of an intracanalicular adenofibroma, with no gland invasion. Complete removal was done. Six months later the patient coughed up a piece of tissue. Pathological diagnosis was sarcoma. At about the same time the entire cutaneous area was involved with growths from the size of a French pea to a hazelnut. These were subsequently pronounced sarcoma. The inference is either that the slides were wrongly read by the first pathologist or that the original canalicular growth degenerated into a sarcoma at some point that escaped the pathologist's attention.

As previously stated, my list of operations for cystic breasts does not represent an operative furor: These operations were done for demand reasons—persistent soiling of the linen by leakage; rapid growths; reoperative disappointment and fear of more operations on the part of several who had from two to five removals done which were followed in a short time by palpable recurrences or rather new growths. These in all probability were preëxisting small cysts that enlarged.

In those patients in whom we intend removing a single cyst, but whose breast tissue we find studded with numerous cysts in size just visible to that of a French pea or larger, I advocate amputation of the breast without the extensive dissection done in malignancies.

These patients do not have the feeling of mutilation, as expressed by Bloodgood, and more recently by Peck quoting Bloodgood, but in the majority of instances are grateful for the work done. I feel that if they are to have the operation created in their minds many times by propagandists and annual cancer weeks, newspaper notoriety and so on, that a placid mentality due to a complete operation is far better than diseased mentality with a less radical

[2] Am. Jour. Surg., 1912, **26**, 208.
[3] St. Bartholomew's Hosp. Repts., 1888.

operation, not only for the tumor-bearing individual but also for each of her relatives and friends.

While cancer-week notoriety and propagandism is desirable, nevertheless I have found from my office experience that a great deal of unnecessary mental suffering is created during these periods which again is followed by the gratitude of the sufferer whose mind is relieved.

In the single growth, the blue-dome cyst of Bloodgood, the discrete fibroma and the canalicular growths, the operation of removal resolves itself into a resection of the area well outside the tumor, with proper suture repair.

Conclusion. In conclusion I should like to emphasize the belief on my part.

1. That no tumor in the breast is a desirable tenant, even if its innocence be proven without a question of doubt.

2. That a growth in the remaining breast is as likely to be of primary origin as was that in the breast first removed.

3. That at the present day we are unable to state positively what the influence of roentgen-ray and radium is either as a preoperative or postoperative aid. But in view of many apparent reductions in size, previous to operation in cases considered nonoperable, the use of roentgen-ray and radium should be encouraged until proven a menace. In my opinion too few years have passed for positive results to be shown even in view of some of the glowing reports at present regarding the non-recurrence. Postoperative treatment should not be neglected by preoperative until some definite proof of its help or inefficiency has been established.

4. That in the presence of late metastases the powerful currents of the present day should be given a thorough test to prove or disprove the efficiency of this method of treatment.

5. That the most thorough and painstaking wide removal with remote glandular and fascial dissections will tend more and more to increase our percentage of cures and extension of life. That the radical operation is attended with so low a mortality as to promote a greater desire on the part of consulting physician to demand early operation.

THE RESULTS OF OPERATIONS FOR CHRONIC APPENDICITIS (SECOND SERIES.)

By Charles L. Gibson, M.D.,

SURGEON TO THE FIRST (CORNELL) SURGICAL DIVISION, NEW YORK HOSPITAL, NEW YORK.

This paper is supplementary to one published in this Journal in 1920,[1] which set forth the results of operations for chronic appendi-

[1] Am. Jour. Med. Sci., 1920, **159**, 654.

citis in my ward-service of the New York Hospital from January, 1913, to July, 1919. In that paper it was pointed out that we had too large a proportion of unsatisfactory results. It was, however, shown that better results were obtained in the last year and that the earlier results fell into a period of reorganization and the preparation for and active participation in the World War. The better results began to show so soon as we were able to analyze the causes of our failures and apply better methods.

TABLE I.

Year.	Number of cases.	Unsatisfactory, per cent.
IODIN PREPARATION.		
1913	70	28
1914	63	23
1915	98	28
1916	100	26
1917	119	24
1918	84	20
PICRIC ACID PREPARATION.		
1919	68	13
1920	97	19
1921	105	6
1922	126	7
1923	79	8

This second series represents a period of stability and an earnest endeavor to improve our methods. It has been most satisfactory to find that the beginning improvement noted in our first paper has been maintained and improved, and we have only 9 per cent of unsatisfactory, a 50 per cent improvement.

Our results have been studied with careful attention to the lessons of our follow-up system which has now been in operation eleven years. This last series shows only 5 per cent without follow-up report, a remarkable showing for a hospital service with many recent immigrants who quickly scatter. Table II gives a comparison of the results.

TABLE II.—COMPARISON OF THE TWO PERIODS.

Results.	January 1, 1913, to July 1, 1919. No.	Per cent.		July 1, 1919, to January 1, 1924. No.	Per cent.	
A. Excellent	259	46.0	58	283	62.0	85
B. Satisfactory	65	12.0		105	23.0	
C. Unsatisfactory	102	18.0		41	9.0	
D. Unknown	126	23.0		22	5.0	
E. Deaths	3	0.5		3	0.7	
Total	555			454		

NOTE.—In the second series the unsatisfactory results have been cut down 50 per cent.

Our routine procedure comprises a reëxamination by the operator in person after three months. Whatever the result, the patients are told to come back any time they like if they have any complaints, so some of our notes extend over a period of years. Patients with definite complaints (Class C—Unsatisfactory) are usually urged to reënter the hospital for examinations, fluoroscopy, cystoscopy, and so forth. Some of these are relieved by the hospital stay alone, suitable diet, laxatives and suppression of bad liquor; but are still recorded in the unsatisfactory class although subsequently reporting themselves all right.

To get an accurate classification we have adopted a standard, which is in a measure unfair as it gives an exaggerated value to irrelevant complaints.

Class A, Excellent, applies only to patients who make absolutely no complaint; a condition hard to attain, as many of these people are naturally a discontented and complaining lot.

Class B, Satisfactory. The patient has some complaint; but not directly connected with the operation, *e. g.*, constipation, a normal condition for these sedentary sweatshop workers.

Class C, Unsatisfactory. All those having definite complaints, even if we believe they are liars or neurotics, as many are. For instance a girl fat and rosy, who has gained forty pounds; but claims to vomit daily, is included in this class.

In the first paper I formulated the following rules: "To avoid disappointing results after operations for chronic appendicitis, I recommend:

"1. A comprehensive and detailed history.

"2. A complete and thorough physical examination, including all refinements of diagnosis.

"3. Exercise caution in undertaking operation on women as compared to men.

"4. Exercise caution, particularly in the more mature patients, particularly women. In this class other lesions may coëxist or may be mistaken for appendicitis.

"5. Avoid the neurasthenics of any age or sex.

"6. Exercise particular restraint when there is no clear and reliable history of well-defined attacks, particularly of localized pain accompanied by nausea or vomiting.

"7. Make a good-sized incision, and, even if a frankly pathological appendix is found, look for other possible lesions.

"8. If no obviously pathological appendix is found, do not cease looking for other lesions until every other possibility has been exhausted; make a supplementary incision if necessary."

From a study of the second series we feel we have nothing to take back in these conclusions, and while essentially no new knowledge has been acquired, the value of the rules has been emphasized. Table III gives comparative statistics of some of the main lines of observation.

TABLE III.—COMPARISON OF TWO PERIODS.

Items analyzed.	Percentage.							
	Excellent.		Satisfactory.		Unsatisfactory.		Unknown.	
	1919.	1924.	1919.	1924.	1919	1924.	1919.	1924.
A. Male	70.0	69.0	14.0	17.0	16.0	9.0	..	5.0
Female	56.0	58.0	16.0	26.0	28.0	11.0	..	5.0
B. History of well-defined attacks	51.0	47.0	51.0	48.0	35.0	18.0	47.0	41.0
C. Kind of incision:								
McBurney	37.0	1.0	22.0	0.0	31.0	0.0	52.0	0.0
Large	63.0	99.0	78.0	100.0	69.0	100.0	48.0	100.0
D. Average number of days spent in hospital	2.6	1.7	2.5	2.1	3.2	2.2	2.3	1.4
E. Special examinations	46.0	17.0	54.0	24.0	56.0	36.0	36.0	18.0
F. Appendix diseased	85.0	96.0	75.0	95.0	63.0	84.0	77.0	90.0
G. Further exploration	52.0	80.0	83.0	89.0	73.0	84.0	52.0	90.0
H. Subsequent admission	2.0	2.0*	0.0	0.9*	25.0	32.0	2.0	0.0
I. Subsequent operation	1.5	1.0*	0.0	0.0	5.0	4.0	2.0	0.0

* Admitted and operated on for conditions in no way related to appendix, *i. e.*, cellulitis of foot.

Of the unsatisfactory cases, 32 per cent were male and 68 per cent were female.

Total number of male cases, 164. Of this number, 14 cases (9 per cent) were unsatisfactory. Total number of female cases, 290. Of this number, 30 cases (11 per cent) were unsatisfactory.

Total number of unsatisfactory cases, 44. Of this number, 14 cases were male (32 per cent); 30 cases were female (68 per cent).

Item A. It will be noted that women continue to give the most unsatisfactory results. This fact we knew from our earliest studies and tried diligently not to fall into this obvious trap. We feel that the proportion of so-called chronic appendices in women should be diminished to approximate more nearly the ratio of operations for acute appendicitis in the two sexes.

Item B. Shows the importance of a definite intelligent history of previous attacks. In our latest series of unfavorable results (Class C), only 18 per cent gave this clear-cut picture.

Item C shows the disappearance of the McBurney incision, all our operations permit of thorough exploration.

Item D shows that patients were kept longer under observation for the same reason as given in item E.

Item E shows that more examinations were made in the unsatisfactory (fluoroscopy, cystoscopy and so forth), these being the cases in which the clear-cut histories were wanting.

Item F bears out the observation of our first series, that in the unsatisfactory cases the appendix is less often recorded in the operative dictation as being distinctly pathological. We have, however, a gratifying increase, 84 per cent, over 63 per cent of our first series.

Item G shows the great increase in the amount of exploration as recorded in the dictation of the operation in our second series—made possible by a proper incision. This is probably a most important factor in the improved results.

Item H shows that an important percentage of our unsatisfactory results were readmitted for investigation or treatment; but item I shows that only in a very small percentage were indications for another operation established.

A comparison of the postoperative complaints of the Class C patients (Table IV) shows no essential difference in the two periods (102 cases in first period, 41 in second). Pain of some kind is the constant complaint. Pain of course is hard to check up; we have no means of denying or corroborating the patient's story. One feature that is disconcerting is the percentage of these Class C patients complaining of the "same pain as before operation" (19 per cent for 1919, 43 per cent for 1924). The complaints fall into two main groups, same pain as before operation and gastro-intestinal complaints.

TABLE IV.—POSTOPERATIVE COMPLAINTS OF UNSATISFACTORY CASES. CLASS C.

Same pain as before operation (4 male and 14 female)*	18
Gastro-intestinal complaints (3 male and 9 female)	12
Pains everywhere	2
Numerous complaints	2
Gynecological conditions	4
Pain in upper right quadrant	1
Pain in upper end of scar and sometimes around ribs and chest	1
Pain over kidney region	1

* Same pain as before operation, 1st series, 1919, 19 per cent; same pain as before operation, 2d series, 1924, 43 per cent.

Class D, Unknown. There was a gratifying decrease in this class in the second series.

Class E, Deaths. (Three cases in second series).

CASE I.—L. C., male, aged thirty-four years. Appendix diseased. Exploration negative. Developed consolidation at the base of the left lung. Transferred to the Medical Side. Temperature began to remit and condition of patient became quite satisfactory. On the fourteenth postoperative day he suddenly developed dyspnea and complained of a pain in his chest. Died in five minutes. Autopsy showed embolism of pulmonary artery, thrombosis of right internal iliac and infarct of lung.

CASE II.—A. S., male, aged thirty-four years. Appendix not diseased and exploration negative. Convalescence uneventful until ninth postoperative day when the patient got up. He became

cyanotic with great air-hunger and died in fifteen minutes. Autopsy showed thrombosis in left internal iliac with a pulmonary embolus at the bifurcation of the left pulmonary artery.

CASE III.—H. D., male, aged thirty-five years. Appendix diseased. Exploration negative. On the second day following operation the patient began to have acute pain and signs of peritonitis. Revision of first operation: diffuse peritonitis. The source could not be ascertained. Jejunostomy and drainage. The patient died shortly after leaving operating room. No autopsy.

Summary. Attention was called in our first paper to the coincidence of our beginning better results with the replacement of tincture of iodin by picric acid as a skin disinfectant, introduced in the last half of 1918 and continued to date. We believe it may be a feature (perhaps important) of our continued improvement, as it is less irritating and less easily carried into the peritoneal cavity.[2] We note it is coming more into general use.

We believe that unsatisfactory results in surgical practice may be greatly diminished if the will to do better work is established. We believe that a most important factor is the creation of a workable standard on which to base results, a careful analytical study of the causes of poor results and the unflagging desire and search for better methods. If these requirements are fulfilled, better results will more than repay all extra effort.

THE PRESSURE FACTORS IN THE BILIARY-DUCT SYSTEM OF THE DOG.

BY A. WINKELSTEIN, M.D.,

AND

P. W. ASCHNER, M.D.,

NEW YORK.

(From the Surgical Laboratories of the College of Physicians and Surgeons, Columbia University.)

Introduction. The mechanism effecting the intermittent discharge of bile into the duodenum of man is a problem of great interest. Many of the factors involved have been subjected to experimental study in the dog whose biliary system resembles closely that of man.

[2] Gibson, C. L.: The Advantages of Picric Acid over Tincture of Iodin for Disinfection of the Skin, Ann. Surg., 1919, **69**, 127. Farr, C. E.: Picri Acid in Operative Surgery, Ann. Surg., 1921, **73**, 13.

The part which the gall-bladder takes in this mechanism is the chief point of the divergence of opinion in such experimental studies.

Recently one of the authors concluded from the result of experimental studies[1, 2, 3] that the intra-abdominal pressure seems to be the most important agent in effecting the flow of bile from the gall-bladder into the duodenum of the dog. Apparently the entire problem of the biliary flow is bound up with the question of the differential pressures existing in the biliary system. For instance, it is not enough to know that the gall-bladder has tonus variations or that its musculature is capable of contracting on its contents. The question is whether the pressure obtainable is actually large enough to expel part or all of its content. In other words the quantitative variations in the pressures existing in various parts of the biliary system and their relations to each other form the problem of the mechanics of the biliary drainage.

We have attempted, therefore, to study these various pressures experimentally considering: (*a*) The common and cystic ducts, (*b*) the sphincter of Oddi, (*c*) the gall-bladder; (*d*) reciprocal or contrary innervation, and (*e*) the intra-abdominal pressures. The experiments will be briefly recorded.

The Pressure in the Common Duct. *Experiment 1.* May 24, 1923. Young female dog (3257), weighing 7 kilos; ether anesthesia; cystic duct tied. A small glass T cannula was placed in the common duct, and connected with an upright calibrated manometer.

Readings: 60 to 65 mm. bile.

Pilocarpin, gr. $\frac{1}{12}$ given subcutaneously and observations taken for a half hour.

Readings: 60 to 70 mm. bile.

Experiment 2. Same animal. Abdominal wound closed tightly about the upright manometer and respiratory fluctuations noted. Types of respiration imitated by varying the depth of the anesthesia and by manual compression of the lower thorax and abdominal wall. (*a*) Shallow respiration: fluctuation in the height of bile column, 3 mm.; (*b*) Forced respiration: fluctuation in the height of bile column, 6 mm.

Discussion. It is apparent that the pressure in the common duct is rather low; furthermore this pressure varies little, being only slightly influenced by pilocarpin and respiration.

The Tonus of the Sphincter of Oddi. *Experiment 3.* May 4, 1923. Male dog (3323), weighing 13 kilos; ether anesthesia. A cannula, directed toward the duodenum, was placed in the common duct and connected with one arm of a calibrated manometer. To the other arm was attached a syringe filled with warm normal saline,

[1] Winkelstein, A.: Klin. Wchnschr., 1923, **2**, 406.
[2] Winkelstein, A.: Ztschr. f. Exper. Med., 1923, **24**, 127.
[3] Winkelstein, A.: Jour. Am. Med. Assn., 1923, **80**, 1748.

dyed with methylene blue. This apparatus is similar to the one recently used by Mann and Giordano.[1]

The duodenum was opened by a longitudinal incision opposite the papilla of Vater. The colored saline was forced up in the manometer until a drop appeared at the papilla. Readings were taken. Various substances were placed in the duodenum on the papilla, allowed to remain there five minutes, and then aspirated. Following the readings, the papilla was flushed with warm normal saline.

TABLE A.

Substance.	Where applied.	Pressure (saline, mm.).
Normal contents	Duodenum	330
Normal saline	"	330
Magnesium sulphate (25 per cent)	"	220
Hydrochloric acid (N/10)	"	330
Glucose (2 per cent)	"	240
Peptone (1 per cent)	"	240
Cottonseed oil	"	220
Bile salts (10 per cent)	"	260
Benzyl succinate	"	260
Potassium carbonate (10 per cent)	"	160
Calcium chlorid (10 per cent)	"	460
Adrenalin (1 cc, 1 to 2600)	Subcutaneously	150
Pilocarpin (gr., 1/12)	"	250
Atropin sulphate (gr., 1/100)	"	100

Experiment 4. May 11, 1923. Young female dog (3339), weighing 15 kilos. Procedure as in Experiment 3.

TABLE B.

Substance.	Where applied.	Time (minutes).	Pressure (saline, mm.).
Normal contents		20	135
Adrenalin (1 cc, 1 to 2600)	Subcutaneously	2	130
		4	115
		6	105
		8	100
		10	102
		15	108
		20	105
		25	128
		30	134
Atropin sulphate (gr. 1/100)	Subcutaneously	2	132
		4	130
		6	110
		8	115
		10	110
		15	135
		20	135
		23	137
Magnesium sulphate (25 per cent)	Duodenum	3	118
		6	110
		9	120
		12	125

[1] Arch. Surg., 1923, **6**, 1.

Experiment 5. May 18, 1923. Young male dog (3348), weighing 9 kilos. Procedure as in Experiment 3.

TABLE C.

Substance.	Where applied.	Time (minutes).	Pressure (saline, mm.).
Normal contents	Duodenum	20	110
Pilocarpin (gr. 1/12)	Subcutaneously	2	115
		4	120
		6	125
		8	125
		10	130
		15	110
Atropin sulphate (gr. 1/100)	Subcutaneously	1	115
		3	110
		5	105
		6	105
		8	110–120

Experiment 6. June 7, 1923. Young female dog (3382), weighing 10 kilos. Procedure as in preceding experiment.

TABLE D.

Substance.	Where applied.	Time (minutes).	Pressure (saline, mm.).
Normal contents	Duodenum	20	140
Magnesium sulphate (25 per cent)	Duodenum	5	120
		10	125
		12	125
		14	115
		16	110

Discussion. (*a*) Concerning spontaneous variations in the tonus of the sphincter. These are apparently slight as evidenced by the constancy of the repeated readings for fifteen to thirty minutes at the beginning of each experiment. Furthermore, the sphincter shows a tendency to return quickly to its original tonus after a stimulating or inhibiting influence has been exerted.

(*b*) Concerning foodstuffs. The substances usually present in gastric chyme (fat, dextrose, peptones) reduce the tonus when placed on the papilla of Vater.

(*c*) Concerning certain chemicals. Magnesium sulphate, potassium carbonate, and bile salts, lessen the tonus when placed on the papilla of Vater. Calcium chlorid increases the tonus.

(*d*) Pilocarpin increases, while atropin and adrenalin decrease sphincter tonus when administered subcutaneously.

(*e*) It seems difficult to lower the tonus of the sphincter very much. In most cases, the reduction averaged only one-sixth to one-fifth of the original figure. The lowest reading in any case was 90 mm.

The Cystic Duct. It has been suggested that the spiral valves of Heister, present in the cystic duct, may offer an appreciable resistance to the entrance and exit of bile. This was investigated

by Mann[1] who found that these mucosal ridges cause only a maximal resistance of 30 mm. of water. One of the authors[2] observed that when the common duct in a dog under ether anesthesia was cut across, a pressure on the gall-bladder merely of 15 mm. of water was sufficient to express bile through the cystic duct. It was thought unnecessary to repeat these experiments.

The Tonus of the Gall-bladder. In these experiments it was attempted to obviate as possible sources of error, the influence of respiration, circulatory changes in the liver, and the varying amount of bile entering the gall-bladder, by stripping the fundus of the gall-bladder away from its liver bed and carefully ligating the cystic duct without tying off the cystic artery. The following experiment (Experiment 7) demonstrates the disturbing influence of respiration when the fundus is not stripped from the liver.

Experiment 7. May 24, 1923. Young male dog (3357), weighing 7 kilos; ether anesthesia; calibrated upright glass manometer attached to a cannula in the gall-bladder. The fundus was not stripped from the liver and the cystic duct was not ligated.

Readings:

	Expiration (bile, mm.).	Inspiration (bile, mm.).
Cystic duct open	25	40 to 45
Cystic duct closed by ligature (Observations for a half hour.)	15	20 to 25

Pilocarpin, gr. $\frac{1}{12}$, given subcutaneously.

Reading fifteen minutes later: 60 mms. of bile. (At expiration, cystic duct occluded.)

Experiment 8. July 26, 1923. Young male dog (3395), weighing 15 kilos. The fundus of the gall-bladder was stripped away from the liver and the cystic duct ligated.

TABLE E.

Substance.	Time (minutes).	Pressure (bile, mm.).
Before using drugs	25	60 to 65
Pilocarpin, gr. 1/12 (subcutaneously)	10	80 to 90
	12	80 to 90
	14	70 to 75
Atropin, gr. 1/100 (subcutaneously)	8	50 to 55
	17	65 to 70
Adrenalin, 1 cc, 1 to 2600 (subcutaneously)	15	65 to 70

Discussion. It seems that the changes in the pressure within the gall-bladder due to the action of its musculature are very small. Qualitatively these results confirm the experiments of Lieb and McWhorter[2] who, using isolated strips of the gall-bladder wall, found that pilocarpin increased the tonus while atropin and adrenalin decreased it.

[1] New Orleans Med. and Surg. Sour., 1918, **71**, 80.
[2] Jour. Pharm. and Exper. Therap., 1915, **7**, 83.

Reciprocal or Contrary Innervation. In Experiments 3, 4, 5, 7 and 8, the effect of drugs acting either on the gall-bladder or the sphincter of Oddi was studied. Apparently, pilocarpin increases while atropin decreases the tonus of both. It seemed desirable to attempt a study of the simultaneous variations in the tonus of both gall-bladder and sphincter.

Experiment 9. May 18, 1923. Young male dog (3348), weighing 9 kilos; ether anesthesia. A cannula was placed in the common duct as in Experiment 3 and the duodenum opened. The fundus of the gall-bladder was stripped from the liver and the manometer was inserted as in Experiment 7. The cystic duct was carefully ligated avoiding the cystic artery. Pilocarpin and atropin were injected successively, and simultaneous observations on sphincter and gall-bladder tonus were made.

TABLE F.

Substance.	Time (minutes).	Pressure. Gall-bladder (bile, mm.).	Pressure. Sphincter (saline, mm.).
Without drugs	20	25 to 30	110
Pilocarpin, gr. 1/12 (subcutaneously)	5	20 to 25	135
	7	25	115
	8	25 to 30	110
	10	30	120
Atropin, gr. 1/100 (subcutaneously)	1	40	115
	3	45	110
	5	10 to 15	105
	6	10 to 15	105
	8	20	110 to 120

Experiment 10. June 11, 1923. Young female dog (3384), weighing 8 kilos. Procedure as in preceding experiment. Magnesium sulphate applied in the duodenum over the papilla of Vater.

TABLE G.

Substance.	Time (minutes).	Pressure. Gall-bladder (bile, mm.).	Pressure. Sphincter (saline, mm.).
Without drugs	15	20 to 25	110
Magnesium sulphate (25 per cent)	2	20	100
	4	20	100
	10	20	90
	14	25	110

Experiment 11. May 16, 1923. Young male dog (3346), weighing 13 kilos; without anesthesia. Atropin gr. $\frac{1}{100}$ given subcutaneously; ten minutes later adrenalin (1 cc. of 1 to 2600) given subcutaneously. Under ether anesthesia, the abdominal cavity was opened at once. The gall-bladder was found normally distended with 15 cc. of dark viscid bile. The duodenum did not contain any bile similiar to that found in the gall-bladder.

Discussion. It may be concluded from these experiments that atropin decreases and pilocarpin increases simultaneously the tonus of both structures. Magnesium sulphate decreased the tonus of the sphincter without affecting the tonus of the gall-bladder.

In the qualitative experiment (Experiment 11) performed to study opposing innervation, after atropin (to relax the sphincter), adrenalin (theoretically to contract the gall-bladder?) did not effect an expulsion of the gall-bladder content.*

The Intra-abdominal Pressure. *Experiment 12.* Young male dog (3257), weighing 7 kilos, ether anesthesia. The cystic duct was ligated. A cannula was placed in the gall-bladder and a cannula in the common duct and both connected with calibrated upright manometers. The abdominal wall wound was closed tightly about them. The variation with respiration was observed in the column of bile. The depth and force of the respiration was altered by the degree of anesthesia and by pressure exerted manually on the abdomen or lower thorax.

TABLE H.

	Gall-bladder (bile, mm.).	Common duct. (bile, mm.).
Shallow respiration	40	3
Moderate respiration	80 to 100	6
Forced respiration	100 to 120	6

Experiment 13. Same animal as in Experiment 3 (3323). A piece of rubber tubing, in imitation of the common duct, was placed *in situ* and connected with a water manometer. The fluctuations observed were approximately the same as above.

Discussion. The above experiments demonstrate that there exists a large difference in the effect of the intra-abdominal pressure on the contents of the gall-bladder as compared with the effect on the contents of the common duct. In the latter the fluctuation produced by respiration is so slight as to be practically negligible. In the gall-bladder, however, an inspiration may cause a rise in pressure equivalent to three or four times the level which is normally maintained by the tonus of its wall. Furthermore, the pressure reached as a consequence of the respiratory squeeze is nearly twice that which was obtainable by extreme pharmacological stimulation such as the administration of pilocarpin (Experiments 7 and 8).

Summary of the Experimental Results. 1. The pressure in the common duct is relatively low, 60 to 65 mm. of bile, and varies but little.

2. Various agents (notably substances present in gastric chyme and magnesium sulphate) when placed on the papilla of Vater

* It is possible that there is an opposing innervation between the sphincter of Oddi and the pylorus. In a single experiment in which a small rubber balloon was placed in the pylorus, it was observed that adrenalin raised the pressure in the pyloric ring.

lessen somewhat the tonus of the sphincter of Oddi but usually not more than one-fifth to one-sixth of the original figure.

3. Of the drugs acting on the vegetative nervous system, atropin decreases and pilocarpin increases the tonus of both the gall-bladder and the sphincter of Oddi. Adrenalin decreases the tonus of the sphincter.

4. The musculature of the gall-bladder displays tonus variations but seems to possess little contractile power.

5. Contrary or reciprocal innervation or action between the gall-bladder and the sphincter of Oddi could not be demonstrated.

6. Increased intra-abdominal pressure, chiefly due to the inspiratory phase of respiration, effects a large pressure variation within the gall-bladder and almost none in the common duct.

BONE MARROW AND SPLEEN IN THE TREATMENT OF ANEMIA.*

By Chauncey D. Leake, Ph.D.,

and

Joseph S. Evans, M.D.,

Madison, Wis.

(From the Departments of Pharmacology and Clinical Medicine of the University of Wisconsin Medical School.)

A consideration of the unsatisfactory results so often encountered in the traditional symptomatic treatment of various types of anemia by means of iron and arsenic led to a search for a more certain and reliable method of stimulating blood production. It has been shown by Whipple and his associates,[1] in a series of carefully controlled experiments, that neither iron nor arsenic exerts any significant effect on the curve of hemoglobin regeneration following simple anemia. In the opinion of these authors, diet is the most important factor in promoting hematopoiesis. Partial confirmation of this work was published by Musser,[2] who found that iron was of no value in stimulating blood formation in hemorrhagic anemia.

With detailed reports on their experimental studies, Hammett and his co-workers[3] have advanced claims for germanium dioxide

* We desire to thank the following members of the staff of the Medical School for their hearty coöperation with us in the treatment of cases: Dr. W. S. Middleton, Dr. H. K. Tenney, Jr., Dr. R. C. Blankinship, Dr. R. R. Van Valzah, and Dr. H. M. Kay. We wish also to acknowledge our indebtedness to the careful technical work of Miss E. Kandell and Miss E. Thewlis.

A preliminary notice of this report was published in the Wisconsin Medical Journal in December, 1923.

as an efficient erythropoietic agent. Kast, Croll, and Schmitz[4] found this substance satisfactory in clinical practice, and Lenker[5] became enthusiastic over its effects in secondary anemia. Alexander,[6] however, noted that it was inferior to arsenic and iron in pernicious anemia, while Minot and Sampson,[7] as a result of their carefully conducted studies, could find no improvement in any type of anemic condition in which it was used. Further critical experimental investigation of germanium dioxide in animals by Bailey, Davidson and Bunting[8] has shown that the early reports on its erythropoietic action cannot be substantiated. Although careful experimentation cannot as readily dispose of iron and arsenic as hematopoietic agents in the face of their long and successful clinical use as such, one is fully justified in seeking a more efficient and rapid means of promoting hematopoiesis.

As a way of approach to the problem, the following line of reasoning was tentatively adopted, which may be quoted from a previous publication:[9]

"(*a*) The production of red blood cells is not constant and maximum for existing red bone marrow, but, more in accordance with the general economy of nature, is regulated by the rate or extent of erythrocyte destruction, and a margin of reserve remains for the functioning of existing red bone marrow, with extension of the erythrogenic centers occurring only when this margin of reserve is exhausted under conditions of extraordinary stress; (*b*) the spleen, usually accepted as the organ chiefly concerned with the removal of the older erythrocytes from the circulation, elaborates, in proportion to the number of red blood cells removed, and possibly from them, a hormone capable of stimulating erythrocyte production; (*c*) this splenic hormone, being carried by the blood, lodges in the erythrogenic centers of the red bone marrow, either by means of an affinity of its own for them, or through the agency of a receptive substance in them capable of binding it, and (*d*) under the influence of this combination, and possible with the destruction of the hormone or hormones concerned in the process, the activity of the adult erythropoietic system is regulated."

We are aware that various portions of this hypothesis conflict with the opinions of certain authorities,[10] but it is compatible with the schema of the "hemolytopoietic system" as outlined by Krumbhaar,[11] and it was found to be convenient as a working theory.

Preliminary experimentation on dogs and rabbits, with adequate control studies, showed that splenic and red bone marrow extracts were powerful erythropoietic agents, and that they were more effective in combination than when used separately.[9] The experiments indicated that these preparations acted first by increasing the rate of production or delivery in existing erythrogenic centers, and secondly by causing an extension of functioning red marrow.

Further experimentation on normal humans[12] confirmed these results and led to the belief that these materials when used in combination might prove helpful in certain types of anemia. It was shown that desiccated preparations were effective, and that they could be administered in capsule form. Not only was a marked rise noted in the number of circulating red blood cells (amounting to over 15 per cent in the case of the combined materials), but the hemoglobin content was also found to be considerably increased. Although this rise in the hemoglobin was not as rapid nor as great as the erythrocytic increase, it was better maintained when administration was stopped. Since the percentage of reticulocytes was much higher under the influence of the combined desiccated marrow and spleen, increased bone marrow activity was indicated. The increase in the number of reticulocytes, however, was not sufficient to account for the increase in red blood cells, so that some other factor, possibly augmented resistance to hemolytic processes, must have been involved. It was also noted that the absolute number of polymorphonuclear neutrophiles was raised, that the blood volume did not change, and that there were not untoward accessory actions.

It has been pointed out[13] that there is no compelling logic in the argument that because certain cells are formed in a special tissue, the latter must abound in available chemical stimulants for the productive activity in question. Furthermore, in view of this consideration, critical therapeutists have looked with doubtful approval on the proposals to use preparations of spleen and bone marrow as blood stimulants in anemia. It was stated that experience with numerous failures of vaunted hematopoietic agents warns against undue early enthusiasm when some new findings is announced. We have felt fully the force of these declarations and hence have subjected the experimental results to most careful scrutiny before undertaking clinical work. It is hardly necessary to indicate that the experimental studies only indirectly lend support to the hypothesis from which we started.

As has been inferred, many proposals have been made to use preparations of bone marrow and spleen for hematopoiesis in anemia. None of these, so far as we know, were based upon critical experimental work. Many scattered reports have appeared on the empirical use of such preparations in anemic conditions, and it may be of interest briefly to review the more important of these.

Red Bone Marrow. The use of red bone marrow in the treatment of anemia is nothing new. Osler and McCrae[14] pointed out that it has the merit of a recommendation by Galen, and, indeed, during the last decade of the nineteenth century it came into widespread clinical use, only gradually to be discarded as newer methods of treating anemia gained prominence, and as new technic was introduced in the administration of iron and arsenic.

During this period, aside from an isolated experimental statement by Danilewsky and Selensky,[15] the use of red bone marrow in the treatment of pernicious and secondary anemias rested almost entirely upon an empirical basis. According to Quine,[16] Brown-Sequard and D'Arsonval in 1891 first suggested it as a remedy in conditions of defective hemogenesis. The first clinical paper on its effects appeared in 1892, by Kast and Rumpel,[17] who used it in pernicious anemia. Within the next few years a considerable number of reports were made, in which red bone marrow was described as a valuable agent in effecting an improvement in various types of anemias. Usually saline extracts of freshly obtained red marrow was used, although in some cases glycerin extracts were said to be superior. Oral administration was invariably followed.

Four cases of chlorosis and secondary anemia successfully treated with fresh beef marrow saline extract were reported by Mann.[18] Impetus to its use was given by the Edinburgh pharmacologist Fraser,[19] when he presented a case of pernicious anemia greatly improved after a prolonged course of marrow treatment supplemented with iron, arsenic and salol. Billings[20] made an excellent study of its effects in 2 typical chloro-anemia cases, and in 2 patients suffering from grave pernicious anemia. He favored its use in chlorosis as a result of the great improvement in his 2 cases, in which the erythrocytes increased by a million cells within a month, and in which the hemoglobin percentage rose markedly, but not in proportion to the increase in red cells. In the cases of pernicious anemia, however, he noted an initial rise in erythrocytes and hemoglobin, followed by a gradual decline, and he cautioned against its use in this condition, pointing out that claims for improvement following the administration of red marrow in pernicious anemia must be carefully weighed in view of the difficulty of accurate diagnosis. An instance of this character was Danforth's report[21] of the cure, by marrow and arsenic, of a case of apparent pernicious anemia, which eventually was shown to be malaria, and which ended fatally. Hamilton's paper,[22] in which announcement was made of the prompt cure of 21 cases of severe anemia by glycerin bone-marrow extract can only be construed as an enthusiastic exaggeration. A report was made by Aleksieyeff,[23] however, that bone marrow was an excellent blood-producing agent in various chronic and wasting diseases. Barrs[24] had 1 case of pernicious anemia in which red bone marrow gave great improvement after arsenic had done no good, even though it had been pushed to the point of manifesting symptoms. In another instance, however, marrow alone resulted in no betterment. Drummond[25] found some gain under marrow in pernicious anemia, but it was much more marked when supplemented with arsenic. Contrary to most findings, Stockman[26] noted that both the erythrocytes and the hemoglobin fell under marrow treatment in pernicious anemia. In an excellent

review of the situation, Hunt[27] presented 3 cases of pernicious anemia, in whom red bone-marrow treatment resulted in slight improvements in the blood picture, which compared unfavorably, however, with the more striking betterment observed under arsenic. Hunt questioned the rationality of the treatment, doubting that the marrow extract supplied a deficiency, since this would be unlikely in pernicious anemia with an hypertrophied marrow. Hunt intimated that it served as a stimulant to an already overstimulated marrow. One of the last notices of the therapeutic use of red bone marrow in anemia was Brunton's[28] in which he described a marked improvement in a case of pernicious anemia treated with marrow tablets.

It may be of interest to note that a commercial preparation of red bone marrow—a glycerin extract of the material containing 2 per cent protein, 0.1 lecithin, 85 per cent glycerin, and undetermined iron—was admitted to New and Non-official Remedies in 1909,[29] but was subsequently removed.

Spleen. In contrast to red bone marrow, the therapeutic use of splenic extract has received but little attention from clinicians, to judge from the reports made, but the relation of the spleen to blood formation has been the subject of a great amount of experimentation and controversy. Not only has this study been direct in following blood changes after spleen administration, as exemplified by the reports of Danilewsky and Selensky,[15] Goldscheider and Jacob,[30] Simon and Spillman,[31] Brinchman,[32] and Downs and Eddy,[33] but most intensive investigation has been made of the problem indirectly, by a study of the effects of splenectomy on the blood picture. Most independent workers on the matter—Zesas,[34] Pugliesse,[35] Wolferth,[36] Orr,[37] and Hitzrot,[38]—agree more or less with the collaborated work of Austin, Krumbhaar, Musser, Pearce, and Pepper,[39] that splenectomy in normal animals results in (*a*) a slight to moderate anemia lasting from four to twelve weeks; (*b*) a leukocytosis which gradually declines; (*c*) an increased resistance of the erythrocytes to hypotonic saline. Since the anemia following splenectomy is accompanied with a diminution in the number of reticulocytes, Krumbhaar and Musser,[40] believe that the postsplenectomy anemia results chiefly from lessened blood formation, due to the loss with the spleen of a substance which normally stimulates the red bone marrow. This position is opposed by Paton and Goodall,[41] Freytag,[42] Asher,[43] and Gilbert,[44] but it is in accord with the fact that the administration of splenic extract in normal animals is followed eventually by an increase in the red blood cells, as found by Danilewsky and Selensky,[15] Simon and Spillman,[31] Eddy,[45] and as reported previously.[9, 12] No explanation can be made of the leukocytosis following splenectomy,[46] but the increased resistance of the erythrocytes to hypotonic saline after this operation agrees with the observations of Bolt and Heeres[47] that the osmotic resist-

ance of the red blood cells is decreased by the spleen, while their resistance against saponin is increased by passage through this organ.

From a clinical point of view the reports of Carpenter[48] are of interest. He found splenic extract of value in treating typhoid fever and malaria. While he gives no figures, he states that the substance aids by increasing the number of leukocytes. A most interesting comment is made by this author to the effect that if the splenic extract does not produce the desired improvement, it should be combined with red bone marrow. The marrow extract seemed to activate the splenic extract in cases which did not respond to splenic extract alone.

Clinical. *We wish clearly to emphasize that any attempt to promote hematopoieses in anemic conditions is, in general, only symptomatic treatment. No anemia can be considered cured unless the cause for it is determined and eliminated. If the attempt to improve hematopoiesis is successful, the effects of the anemia may be more or less alleviated, but the excessive strain on the blood-producing organs is present, and this cannot be regarded as a healthy situation. The restoration of blood function to normal, however, even if only temporary, may make it possible to attack more successfully the fundamental cause of the anemia by other methods. We hold, then, that the promotion of hematopoiesis in anemia is merely adjunctive to treatment directed toward the discovery and removal of the underlying cause of the condition.*

In evaluating the results of any effort to stimulate erythrocyte and hemoglobin formation in anemic conditions many factors must be considered. As pointed out by Billings,[20] one must constantly keep in mind the difficulties of accurate diagnosis, of accurate estimation of the rate or extent of blood destruction as compared with blood regeneration and of estimating the capacity of an individual to regenerate blood. Moreover, the chronicity of the anemic condition and changes in the metabolic functions of the patient during the course of treatment greatly modify the objective criteria which should be used as a basis of judgment. One must seek rigorously to exclude the possibility of spontaneous improvement under the influence of factors not related to the treatment employed. Only long experience and a large series of carefully kept records, hard to obtain in ambulatory cases, can overcome the difficulty of comparing accurately the treatment in question with other forms of treatment in the same individual or in different patients. Finally, to emphasize the obvious, it is necessary to use the same instruments and technic throughout, and to maintain adequate control over the factors modifying blood concentration and distribution, and over whatever else may influence the blood picture.

In our clinical work on the symptomatic treatment of anemia by desiccated red bone marrow and spleen, we have followed 102 cases. Of this number, 65 are included in the present report as being satis-

factory with regard to the various factors mentioned above. The omission of 37 cases from this report does not in any way hide our failures since all these 37 patients showed improvement during the course of the treatment. They are not considered satisfactory for inclusion here because the possibility of spontaneous remission unrelated to the treatment cannot be excluded from 12, while in 4 the treatment was complicated by the use of other methods, and in the remaining 21, although improvement was noted in the records obtained, the data are not satisfactory because of failure on the part of the patients to return for final examination or for other reasons. All our unsuccessful cases are therefore included in those here reported although in 2 of these a case of anemia secondary to malignant endocarditis and one secondary to chronic tuberculosis, the records are far from satisfactory.

The desiccated spleen and red bone marrow powders, obtained through the courtesy of the Wilson Laboratories, were combined in equal proportions by weight, and were administered in 0.3 gm. (5 gr.) capsules, three times daily, before meals, with plenty of water. With improvement of the blood picture this dosage was diminished at first to 2 capsules and then to 1 capsule daily, the administration being withdrawn as soon as the erythrocyte and hemoglobin content of the blood remained constant.

TABLE I.—SUMMARY OF CASES.

Diagnosis.	Number of cases.	Markedly improved.	Moderately improved.	Slightly improved.	Not improved.
Pernicious anemia	2	..	..	..	2
Secondary anemia, cause unknown	15	4	8	3	..
Secondary anemia, cause known	48	13	22	8	5
Total	65	17	30	11	7

As may be seen from Table I, we have divided our 65 cases into 3 classes on the basis of diagnosis: (1) Primary progressive pernicious anemia, in whom not only were all the classical symptoms present, but in whom the disease ran a rapidly fatal course, with evidence of marked marrow injury, and without indicating an ability to regenerate normal blood; (2) secondary anemia without known cause, in whom the blood picture and symptoms varied from those usually associated with grave primary anemias to those generally considered indicative of mild chloro-anemia, but in whom the condition was more or less chronic, without a rapidly developing downward course, and in whom there was evidence of a substantial ability for normal blood regeneration; and (3) secondary anemia with known cause, in whom the blood picture and symptoms varied markedly, but which were usually those associated with chloro-anemia, and which seemed to depend greatly upon the gravity of

the underlying cause. We included 2 cases of what clinically appeared to be true chlorosis in this group, because, although the real cause is not clearly understood, it is certainly associated with faulty iron metabolism.

Clinically one sees wide variations in the blood picture and symptoms of the anemic individual. At times one may find a decrease due to such determinable causes as acute nasal infections, or digestive disturbances, but in some cases the cause cannot be determined. On the other hand, remissions may occur due to relief from the underlying cause, which may be spontaneous or due to remedial measures. This is especially true in those individuals with a cell and hemoglobin count around the lowest level of what may be considered normal values. A spontaneous remission occurring during treatment may therefore be mistaken for a real improvement due to the therapeutic agent. It was possible, however, to follow 10 of our cases over a period of two years, on the average, with careful clinical records before treatment with desiccated spleen and marrow was instituted. During this period these patients received many kinds of treatment, including administrations of iron and arsenic by various routes, without any significant or rapid change in the general level of their hemoglobin and cell count. We feel, since this level in these cases rose markedly upon the administration of desiccated spleen and marrow, and since the general improvement has been maintained, that we are justified in believing the change to be due to the treatment employed. The only comparison between desiccated marrow and spleen on the one hand, and iron and arsenic on the other, as hematopoietic agents, that we have felt it fair to make is in these same 10 cases.

In accurate hemoglobin and blood-cell determinations, the clinician has objective criteria for the study of anemia that are excellent in every respect if only the factors which may modify them are constantly kept in mind. In the majority of our cases the blood was drawn from both the finger tips and the ear lobes for simultaneous duplicate determinations. By this method, we believe we had a fair control on blood distribution insofar as local conditions in the capillary circulation were concerned. In 4 of our hospital cases we used blood which had been drawn from the median basilic vein for other purposes. Since the experimental work had indicated that marrow and spleen extracts do not have any significant effect on blood volume, we made no such determinations in the clinical cases, but rather insisted that our patients receive a large fluid intake. Blood was drawn from the patients in all cases at approximately the same hour of the day.

The duplicate blood-cell determinations were made with American standard hemocytometers and Levy counting chambers certified by the Bureau of Standards, while the hemoglobin determinations were made in duplicate using the Fleishel-Miescher hemometer, or Dare's hemoglobinometer.

In reporting the progress of our cases, we have used objective criteria only. Reliance was placed chiefly on the blood picture. *If the hemoglobin percentage did not improve by five points, nor the erythrocyte count by 250,000 cells, the case was classified as showing "no improvement." An increase in the hemoglobin percentage between five and ten points, and in the red blood cell count between 250,000 and 500,000 cells, placed the case in the "slightly improved" class. If the hemoglobin percentage rose from ten to fifteen points, and the erythrocyte count from 500,000 to 1,000,000 cells, the case was noted as "moderately improved." An increase in a patient of over fifteen points in the hemoglobin percentage, and over 1,000,000 cells in the red cell count, was considered "markedly improved."* Objective symptomatic criteria, such as dyspnea, cardiac thrills, edema, pallor, paraesthesia, and the like, noted especially in the more severe cases, were relieved in all patients as the blood picture improved. We have, furthermore, included in our cases which showed improvement only those in whom it was maintained or bettered as long as the administration of the desiccated spleen and marrow was continued.

We had 2 cases in which postmortem findings confirmed the diagnosis of primary progressive pernicious anemia. Neither of these showed any improvement in the blood picture under the influence of treatment with desiccated spleen and marrow. In fact, it seemed that the stimulus given the blood forming organs by this preparation was detrimental, in that it led to more rapid exhaustion, since the temporary improvement in the hemoglobin and erythrocyte count was followed by a sudden drop. It is difficult to diagnose between essential anemia of the progressive pernicious type in which the blood forming organs seem definitely to be injured, and grave secondary anemia of unknown cause in which the blood making functions appear to be inhibited or unable to meet the demands upon them rather than permanently damaged. In the treatment with marrow and spleen of the progressive pernicious type there has been a drop in the blood picture after an initial rise, while in the grave secondary anemias no such drop has taken place. The type of reaction, therefore, has been considered of diagnostic value, the preparation being discontinued whenever it failed to produce a positive response.

It may be of interest briefly to present an abridged case history of one of these patients suffering from primary progressive pernicious anemia.

CASE REPORT. The patient, a man, aged fifty-six years, was admitted to the Bradley Memorial Hospital on March 12, 1923, complaining of weakness upon exertion, shortness of breath and swelling in the abdominal region. These symptoms with tingling of the extremities and intermittent attacks of diarrhea, had been

present more or less constantly for the past two years. Upon examination he showed all the characteristic symptoms of pernicious anemia, including stomatitis, dyspnea, ascites, paresthesia of the extremities, cardiac thrills, capillary pulse, lemon-yellow pallor, and characteristic blood picture. The patient refused transfusion because of religious scruples. Treatment with desiccated marrow and spleen was instituted on March 13, with dietary and general hygienic regulations. A table showing the changes in the blood picture as treatment was conducted as follows:

Date.	Erythrocytes.	Leukocytes.	Hemoglobin per cent.
March 12, 1923	930,000	6500	25
March 13, 1923	900,000	6600	25
March 14, 1923	1,350,000	6200	32
March 15, 1923	760,000	4400	23
March 16, 1923	870,000	4600	28
March 17, 1923	950,000	4200	30
March 18, 1923	1,300,000	7200	31
March 19, 1923	1,020,000	6800	28

Treatment with desiccated spleen and marrow was discontinued on March 19. The blood picture continued to fall. Intramuscular injections of arsenic and iron failed to give any improvement at all, and on April 3, the patient died. A postmortem examination by Dr. C. H. Bunting confirmed the diagnosis of primary progressive pernicious anemia.

The other case ran a more prolonged course, but presented essentially the same features insofar as the blood picture was concerned when under treatment with desiccated spleen and marrow.

Secondary anemias without known cause are rather frequently encountered. In some cases the condition is progressive and may become grave. Careful search in such cases may often reveal a hidden focus of infection, the removal of which will clear the situation. In other cases, however, the condition is chronic and holds a stationary course. In these patients a history of severe infection or disorder in years past may be elicited, and it may be supposed that the blood-forming organs have never recovered normal activity from the strain placed upon them during that crisis. In such patients the use of desiccated spleen and marrow has been found to bring about moderate to marked improvement, where long continued treatment with iron and arsenic had been without significant effect. Of the 15 cases of secondary anemia without known cause which we have included in this study, 5 were of the active progressive type, probably due to some hidden focus of infection. Of these 5 patients, 3 were slightly improved under the influence of desiccated marrow and spleen, and 2 were markedly improved. The remaining 10 of this general class were cases of long continued chronic anemia, the cause of which had probably disappeared years previously. Of these cases, 2 showed a marked improvement, and

s a moderate improvement under treatment with marrow and spleen.

A greatly abridged case report of 1 of these patients, briefly presented, may be of interest:

The patient, a married woman, aged sixty-one years, first came under observation at the University Clinic in 1919. At that time she complained of shortness of breath and weakness upon exertion. Careful physical examination revealed nothing significant. Her blood picture at that time was 55 per cent hemoglobin, 3,136,000 erythrocytes, and 7300 leukocytes. Treatment by means of intramuscular injections of iron and arsenic was begun, and continued at intervals for three years, during which time her blood picture slowly improved until in June, 1922, it reached 65 per cent hemoglobin, 3,510,000 erythrocytes, and 7080 leukocytes. Irregular administrations of iron and arsenic were continued for over a year, the last being October 12, 1923. On October 19, 1923, her blood picture was 65 per cent hemoglobin, 3,390,000 erythrocytes, and 6400 leukocytes. On this date treatment with desiccated spleen and marrow was instituted, and the course of her blood picture may be seen in the following table:

Date.	Erythrocytes.	Leukocytes.	Hemoglobin per cent.
Oct. 19, 1923	3,390,000	6400	65
Nov. 9, 1923	4,408,000	8400	75
Nov. 26, 1923	4,300,000	8400	78
Dec. 12, 1923	4,200,000	8100	82

On December 12, 1923, the administration of desiccated spleen and marrow was reduced to one capsule daily. On January 10, 1924, the blood picture was 80 per cent hemoglobin, 4,680,000 erythrocytes, and 6000 leukocytes. Administration was discontinued, and on February 11, 1924 the blood picture was 80 per cent hemoglobin, 4,110,000 erythrocytes and 6700 leukocytes, since then the patient has not been seen.

In Table II may be found a summary of the cases of secondary anemia with known cause which we have included in this report. Marked improvements were most consistently noted in patients suffering from menorrhagic anemia, and in the dietary anemias of infants. Two of the cases of menorrhagic anemia had run a chronic course for many years without relief of the anemic symptoms by means of treatment with iron and arsenic or dietary regulation. These two cases showed marked improvement in the blood picture and in clinical symptoms when treatment with desiccated spleen and marrow was instituted.

Some of the most remarkable results obtained by us in this study were in cases of grave anemias secondary to acute pyogenic infections. The sharp arrest of the downward course of the blood picture, its consequent rapid improvement, and the general better-

TABLE II.—SUMMARY OF CASES OF SECONDARY ANEMIA WITH KNOWN CAUSE.

Diagnosis.	Number of cases.	Markedly improved.	Moderately improved.	Slightly improved.	Not improved.
Chronic arthritis	7	..	6	1	
Menorrhagic	10	3	4	3	
Chronic tuberculosis	6	2	1	1	2
Dietary anemia of infants	5	4	1		
Pyelitis	2	..	2		
Streptococcemia	2	2			
Chlorosis	2	1	1		
Severe Dental and Nasal infection	2	..	2		
Malignant endocarditis	1	..	..	..	1
Chronic endocarditis; hemolytic jaundice	1	..	..	..	1
Lung abscess	1	..	1		
Subacute cholecystitis	1	..	1		
Chronic salpingitis	1	..	1		
Multiple osteomyelitis	1	..	1		
Chronic valvulitis	1	..	1		
Chronic sinusitis	1	1			
Cheilitis exfoliativa	1	..	..	1	
Chronic eczema	1	..	..	1	
Gastric carcinoma	1	..	..	1	
Postoperative menopause	1	..	..	..	1
Total	48	13	22	8	5

ment in the condition of the patient upon the administration of marrow and spleen were striking. A brief presentation of a case in question follows:

A University medical student, aged twenty-three years, was admitted to the University Infirmary on March 8, 1923, complaining of a sore throat. Examination revealed nothing significant except a deeply congested and swollen uvula. The patient stated that he suffered more or less chronically with sore throat. He was placed in bed and symptomatic treatment of the throat was undertaken. Rapid improvement took place, and the patient was to be discharged on the morning of the 16th. At 5:00 A.M. the patient called and complained of weakness and rapid heart-rate. The pulse was 160, with systolic pressure of 110 and diastolic pressure 80. There was no cardiac enlargement. On March 18 there was definite cardiac enlargement, with a soft systolic murmur, and continuation of the foetal rhythm. The cervical lymph glands were tender and slightly enlarged. On March 23, with subsidence of the cardiac involvement, an inflammatory condition of the right ankle was noted. On March 23 a positive blood culture was obtained, the organism being Streptococcus buccalis (viridans). On March 25 pretibial edema was noted on the left leg, with tenderness in both legs below the knees. Roentgen-ray examination revealed nothing significant. On April 5 the right ankle was drained; a green producing streptococcus corresponding in its cultural char-

acteristics to Streptococcus buccalis, being isolated from the pus. By April 11 both knees were involved along with the ankles. Drainage was instituted but the patient was weak and reacted acutely to pain.

The course of the blood picture of this patient before symptomatic treatment with desiccated spleen and marrow was begun, follows:

Date.	Erythrocytes.	Leukocytes.	Hemoglobin per cent.
Mar. 17, 1923 . . .	3,910,000	34,000	84
May 9, 1923 . . .	2,860,000	24,200	63
May 11, 1923 . . .	2,610,000	17,400	60

Treatment was instituted on May 12, the patient having become very weak. The subsequent course of the blood picture with continued treatment follows:

Date.	Erythrocytes.	Leukocytes.	Hemoglobin per cent.
May 16, 1923 . . .	3,810,000	14,200	81
May 18, 1923 . . .	3,840,000	15,400	84
May 22, 1923 . . .	4,010,000	12,600	90
June 6, 1923 . . .	4,490,000	11,300	90

Treatment with marrow and spleen was discontinued on June 6. The blood culture was negative May 22, the patient felt much stronger and was up daily in a wheel chair. Rapid improvement continued, the drainage wounds healed satisfactorily, and the patient was discharged July 7, 1923, with a blood picture of 92 per cent hemoglobin, 4,990,000 erythrocytes, and 10,800 leukocytes.

Of course, the drainage was the main factor of this case. The very rapid improvement in the blood picture in four days, however, and the maintenance of that improvement during the period of continued drainage, with evidence of varying degrees of toxin absorption as shown by the persistence of a remittent and intermittent temperature curve, was most significant of direct stimulation of hematopoiesis by the therapeutic measures employed. This rapid increase in blood formation, we believe, was a factor in this young man's recovery from pyemia.

In a somewhat similar case of streptococcemia quite as pronounced an improvement was noted following the use of desiccated spleen and marrow at a time when the blood picture was steadily falling.

In the dietary anemias of infants, our results were encouraging. The combined materials were administered in these cases as filtered saline broths in amounts appropriate to the age of the child. In these cases the red cell count rose rapidly and immediately, while the hemoglobin increased more slowly. These infants were all less than one year of age. An illustrative case follows:

A male infant, aged five months, was brought to the University Clinic on May 19, 1923. He was pale, emaciated and underweight. He had been bottle-fed since birth on a diet inadequate for his needs. His blood picture was 53 per cent hemoglobin, 2,908,000 erythrocytes, and 6700 leukocytes. Treatment with spleen and marrow broth was begun at once and continued until June 1. By this time arrangements had been made for the adequate regulation of diet and for daily exposure to sunlight.

The course of his blood picture while under observation follows:

Date.	Erythrocytes.	Leukocytes.	Hemoglobin per cent.
May 19, 1923 . . .	2,908,000	6,720	53
May 23, 1923 . . .	4,460,000	9,600	60
June 1, 1923 . . .	4,510,000	11,200	65
June 4, 1923 . . .	4,208,000	10,000	62
July 8, 1923 . . .	4,810,000	9,400	76

Similar improvements were noted in the other cases.

In the rest of our secondary anemias with known cause it may be seen that only moderate improvement occurred in the long-standing chronic conditions, while in the cases of endocarditis, one malignant, and the other chronic with hemolytic jaundice, no improvement at all was noted.

Discussion. We feel that desiccated spleen and red bone marrow constitutes a valuable addition to the armamentarium of the physician in the symptomatic treatment of secondary anemia. It rests upon fair experimental evidence and upon sound, though as yet insufficient, clinical results. Careful critical investigation of its action is forthcoming from independent sources. From reports reaching us from those therapeutists whom we have asked to coöperate with us in testing its clinical value, our results have had a certain amount of confirmation.

The use of desiccated spleen and red bone marrow in the symptomatic treatment of secondary anemia presents many advantages over the more traditional use of iron and arsenic. It lacks the dangers of the toxicity of arsenic, and it avoids the gastro-enteric actions of iron. It is as effective by mouth as by other routes, and the pain, expense, and technical requirements of the intramuscular or hypodermic injections of iron and arsenic, methods preferred because of the surety of absorption, are avoided. Furthermore, it seems to be much more rapid in its influence upon the blood picture, and is certainly as effective. From the subjective symptoms of our patients, and from objective improvements noted, we believe that it has a general therapeutic value in anemia at least equal to that of iron and arsenic.

The possibility that desiccated spleen and marrow are effective in promoting hematopoiesis because of their iron and lecithin contents cannot be denied. This was considered the basis of their action by Danilewsky and Selensky,[15] and later by the Council

on Pharmacy and Chemistry of the American Medical Association when a glycerin extract of red bone marrow was admitted to New and Non-official Remedies.[29] We have determined the iron content of the combined desiccated preparation to be between 2.5 and 3 mg. per gm., using the colorimetric method of Wong.[49] According to Sherman,[50] this would represent about one-tenth of the daily iron intake on an average diet. The lecithin content of the combined desiccated preparation is one-third of egg yolk on the average, or about 30 mg. per gm. Whether these small amounts of iron and lecithin can so profoundly alter the blood picture of normal or anemic humans is a matter of conjecture.

In the preparation of these materials, the spleen is freed from connective tissue and fat before desiccation and powdering. The marrow is obtained from the short ribs of calves, and is dried and powdered after being only partially separated from calcium and fat by gross mechanical means. The calcium content of the desiccated marrow is between 20 and 30 per cent.

We realize that the results of treatment by desiccated spleen and marrow in 65 cases of anemia is not enough to serve as the basis for decisive conclusions, but it is felt that the results are sufficiently encouraging to warrant further careful and critical trial of this method of promoting hematopoiesis in secondary anemia. It is hardly necessary to indicate that this mode of treatment in anemia does not in any manner encroach upon the field of usefulness of transfusion in an emergency or acutely grave condition.

Clinical and experimental observations indicate that the combined preparation of spleen and red bone marrow stimulates cell production, and possibly increases cell resistance. If this assumption is correct, then it is indicated whenever the blood-making function are inhibited or are below the requirements of normal conditions, or whenever there is excessive erythrocyte destruction as in acute or chronic infections.

Summary. A review of the partially successful empirical use of marrow and spleen as hematopoietic agents justified an experimental investigation of these materials, in which it was demonstrated in normal animals and humans that they were more efficient in promoting hematopoiesis in combination than separately.

Desiccated spleen and red bone marrow combined in equal proportions by weight and administered in 0.3 gm. (5 gr.) capsules, has been found beneficial in the symptomatic treatment of secondary anemia, and presents many advantages over iron and arsenic.

In this report, 65 cases of various types of anemia are presented, in which the action of desiccated spleen and marrow has been carefully followed. Of these 65 cases, 47 were moderately to markedly improved with respect to the blood picture and other objective criteria, while 18 showed slight or no improvement. Among these latter are 2 cases of progressive pernicious anemia, the only cases of this class studied by us.

Desiccated spleen and red bone marrow may afford a valuable addition to the armamentarium of the physician in the symptomatic treatment of secondary anemia, and may be of diagnostic value in the differential diagnosis between progressive pernicious anemia and grave secondary anemia. The results thus far seem sufficiently encouraging to warrant further careful and critical trial of this method of promoting hematopoiesis.

BIBLIOGRAPHY.

1. Whipple, G. H., Hooper, C. W., and Robscheit, F. S.: Blood Regeneration Following Simple Anemia, Am. Jour. Physiol., 1920, **53**, 151, 167, 206, 236, 263. Whipple, G. H. and Robscheit, F. S.: Iron and Arsenic as Influencing Blood Regeneration Following Simple Anemia, Arch. Int. Med., 1921, **27**, 591.

2. Musser, J. H. Jr.: The Influence of Inorganic Iron on the Regeneration of Blood after Hemorrhagic Anemia, Arch. Int. Med., 1921, **28**, 638.

3. Hammett, F. S., Nowrey, J. E., Jr., and Muller, J. H.: Erythropoietic Action of Germanium Dioxide, Jour. Exper. Med., 1922, **35**, 173. Muller, J. H., and Iszard, M. S.: Erythropoietic Action, Cumulative Effect and Elimination of Germanium Dioxide, Am. Jour. Med. Sci., 1922, **163**, 364. Hammett, F. S., and Nowrey, J. E. Jr.: Source of Erythrocythemia Produced by Germanium Dioxide in Albino Rat, Jour. Exper. Med., 1922, **35**, 507. Nowrey, J. E., Jr.: Effect of Sodium Germanate Upon the Total Hemoglobin of the Albino Rat, Bull. Johns Hopkins Hosp., 1922, **33**, 340. Muller, J. H., and Iszard, M. S.: The Effect of Germanium Dioxide Upon the Blood, Jour. Metab. Res., 1923, **3**, 181.

4. Kast, L., Croll, H. M., and Schmitz, H. W.: Therapeutic Use of Germanium Dioxide in Anemia, Jour. Lab. Clin. Med., 1923, **7**, 643

5. Lenker, J. L.: Pernicious and Secondary Anemias Treated with Germanium Dioxide, Penn. Med. Jour., 1922, **26**, 86.

6. Alexander, M. E.: Action of Germanium Dioxide in Pernicious Anemia, Am. Jour. Med. Sci., 1923, **166**, 256.

7. Minot, G. R., and Sampson, J. J.: Germanium Dioxide as a Remedy for Anemia, Boston Med. Surg. Jour., 1923, **189**, 629.

8. Bailey, G. H., Davidson, P. B., and Bunting, C. H.: Personal communication to the authors.

9. Leake, C. D., and Leake, E. W.: Erythropoietic Action of Red Bone Marrow and Splenic Extracts, Jour. Pharm. and Exper. Therap., 1923, **22**, 75.

10. Bunting, C. H.: The Regulation of the Red Blood Cell Supply, Contributions to Medical and Biological Research, dedicated to Sir William Osler, 1919, **2**, 824.

11. Krumbhaar, E. B.: The Hemolytopoietic System in Primary Anemias, Am. Jour. Med. Sci., 1923, **166**, 329.

12. Leake, C. D.: Hematopoietic Effects of Desiccated Red Bone Marrow and Spleen in Normal Humans, Jour. Pharm. and Exper. Therap., 1923, **22**, 401.

13. Editorial: Jour. Am. Med. Assn., March 8, 1924, **82**, 797.

14. Osler, Sir. W., and McCrae, T.: Principles and Practice of Medicine, New York and London, 1922, p. 733.

15. Danilewsky, B., and Selensky, M. Uber die blutbildende Eigenschaft der Milz und des Knochenmarks, Arch. f. d. ges. Physiol., 1895, **61**, 264.

16. Quine, W. E.: The Remedial Application of Bone Marrow, Jour. Am. Med. Assn., May 23, 1896, **26**, 1012.

17. Kast, A., and Rumpel, T.: Knochenmark bei pernicioser Anamie, Path. Anat. Tafel Hamb Staats-krank. Wandsbek., 1892, vol. **3**.

18. Mann, J. D.: Extract of Bone Marrow in the Treatment of Anemia, Lancet, 1894, **1**, 599.

19. Fraser, T. R.: Bone Marrow in the Treatment of Pernicious Anemia, Brit. Med. Jour., 1894, **1**, 1172.

20. Billings, J. S.: Therapeutic Use of Extract of Bone Marrow, Bull. Johns Hopkins Hosp., 1894, **5**, 115.

21. Danforth, I. N.: The Clinical History of Pernicious Anemia, Chi. Clin. Rev., 1895–96, **5**, 80.

22. Hamilton, A. McL.: The Use of Medullary Glycerides in Conditions Attended

by a Paucity of the Red Corpuscles and Hemoglobin, New York. Med. Jour., 1895, **61**, 44.

23. Aleksieyeff, F. K.: Bone Marrow as a Blood Producing Agent in Various Wasting and Chronic Diseases, Vrach. St. Petersb., 1895, **16**, 1057, 1091. Abstract furnished by Surgeon-General's Library.

24. Barrs, A. G.: A Case of Pernicious Anemia in Which Arsenical Palsy Had Been Induced Treated by Bone Marrow, Brit. Med. Jour., 1895, **1**, 358.

25. Drummond, W. B.: A Case of Pernicious Anemia Treated with Bone Marrow, Brit. Med. Jour., 1895, **1**, 1085.

26. Stockman, R.: Remarks on the Nature and Treatment of Pernicious Anemia, Brit. Med. Jour., 1895, **1**, 965, 1025, 1083.

27. Hunt, G. B.: On Some Points in Pernicious Anemia with Special Reference to Treatment with Bone Marrow, Lancet, 1896, **1**, 282.

28. Brunton, J.: A Case of Pernicious Anemia Showing Marked-Improvement Under Arsenic and Bone Marrow, Lancet, 1905, **1**, 87.

29. New and Non-official Remedies: Red Bone Marrow Extract, Jour. Am Med.. Assn., June 12, 1909, **52**, 1929.

30. Goldscheider, A., and Jacob, P.: Uber die Variationen der Leukocytose, Ztschr. f. klin. Med., 1894, **25**, 373.

31. Simon, P., and Spillmann, L.: Resherches experimentales sur l'action des injections d'extrait de rate: Reactions du sang, Comp. rend. Soc. de biol., 1906, **60**, 833.

32. Brinchman, A.: Changes in the Blood after Experimental Feeding with Spleen Tissue, Act. Med. Scand., 1920, **52**, 689.

33. Downs, G. W., and Eddy, N. B.: Influence of Splenic Extract on Number of Corpuscles in Circulating Blood, Am. Jour. Physiol., 1920, **51**, 279. Effects of Subcutaneous Injection of Splenic Extract, ibid., 1922, **62**, 242.

34. Zesas, D. G.: Uber Exstirpation der Milz am Menschen und Thiere, Arch. f. klin. Chir., 1883, **28**, 157.

35. Pugliesse, A.: Neuer Beitrag zur Physiologie der Milz: Das Eisen der Galle and des Blutes bei entmilzten Thieren, Biochem. Ztschr., 1913, **52**, 423.

36. Wolferth, C. C.: Blood Changes in Albino Rats Following Splenectomy, Arch. Int. Med., 1917, **19**, 105.

37. Orr, T. G.: Blood Picture Following Experimental Splenectomy, Jour. Lab. Clin. Med., 1917, **2**, 895.

38. Hitzrot, J. M.: The Effects of Splenectomy on the Normal Individual in Certain Pathological Conditions, Ann. Surg., 1919, **67**, 540.

39. Musser, J. H., Jr.: An Experimental Study of the Changes in the Blood Following Splenectomy, Arch. Int. Med., 1912, **9**, 592. Krumbhaar, E. B., Musser, J. H., Jr., and Pearce, R. M.: The Relation of the Spleen to Blood Destruction and Regeneration and to Hemolytic Jaundice, Jour. Exper. Med., 1913, **18**, 119. Musser, J. H., Jr., and Krumbhaar, E. B., ibid., 1913, **18**, 487. Krumbhaar, E. B., and Musser, J. H., Jr., ibid, 1914, **20**, 108. Pearce, R. M., Austin, J. H. and Pepper, O. H. P., ibid, 1915, **22**, 682.

40. Krumbhaar, E. B., and Musser, J. H., Jr.: Effect of Splenectomy on the Hematopoietic System of Macacus Rhesces, Arch. Int. Med., 1923, **31**, 686.

41. Paton, D. N., and Goodall, A.: The Spleen in Relationship to the Processes of Hemolysis, Jour. Physiol., 1903, **29**, 411.

42. Freytag, F.: Beziehungen der Milz zur Reinigung und Regeneration des Blutes, Arch. f. d. ges. Physiol., 1907, **120**, 501.

43. Asher, L.: Die Function der Milz, Deutsch. med. Wchnschr., 1911, **37**, 1252.

44. Gilbert, Q. O.: The Occurrence of Nuclear Changes in the Red Blood Corpuscles Following Splenectomy, Arch. Int. Med., 1915, **15**, 140.

45. Eddy, N. B.: The Internal Secretion of the Spleen, Endocrinology, 1921, **5**, 461.

46. Leake, C. D.: Leukocytic Reactions to Red Bone Marrow and Spleen Extracts, Jour. Pharm. and Exper. Therap, 1923, **22**, 109.

47. Bolt, N. A., and Heeres, P. A.: The Influence of the Spleen on the Red Blood Cells, Nederland, Tijdschr. Geneesk, 1922, **66**, 2259.

48. Carpenter, C. R.: Splenic Extract and the Splenic Function, Med. Rec., 1900, **57**, 273. Therapeutic Action of Splenic Extract in Malarial Infections, ibid., 1906, **70**, 165.

49. Wong, S. Y.: Colorimetric Determination of Iron and Hemoglobin in Blood, Jour. Biol. Chem., 1923, **55**, 421.

50. Sherman, H. C.: Iron in Food and Its Function in Nutrition, U. S. Dept. Agric. Bull. 1907, **185**, 79.

SPLENIC ANEMIA: REPORT OF A CASE IN A LATE STAGE CURED BY SPLENECTOMY.*

By Edmund Horgan, M.D., F.A.C.S.

IN COLLABORATION WITH

William P. Reeves, M.D., F.A.C.S.

AND

William Earl Clark, M.D., F.A.C.P.

WASHINGTON, D. C.

The spleen, found in almost all vertebrates, is one of the chief parts of the lymphatic system. In mammals the spleen is situated in the upper left abdomen; in some of the lower vertebrates it is found in other abdominal regions. In sharks the splenic tissue is found in a number of small masses within the abdomen.

Physiology. The normal physiology of the spleen, or its associated functions with other organs and tissues is not clearly understood, but we know that its function is not essential to maintain the life of the organism, as its removal does not cause death. It is a passively elastic and contractile organ, depending on the amount of blood passing through it. The blood supply is from the splenic artery and the volume of blood which passes into the spleen at the hilum from the several branches of the splenic artery is very great. From the blood which passes through it, toxic substances, bacteria, parasites and disintegrated red-blood cells are removed by the spleen. Phagocytic leukocytes may or may not destroy bacteria and parasites within the spleen. Disintegrated cells, pigment from erythrocytes and toxic substances are carried through the splenic and portal veins to the liver. Here they are further acted upon and eliminated. By a study of the pathological and physiological changes found in diseases of the spleen and the blood, the associated function of the spleen with the liver, bone marrow, and blood has been confirmed.

Regeneration of Blood Cells in the Spleen. The primitive red and white corpuscles are nucleated. In vertebrates below mammals, the nucleus in the erythrocytes is found throughout the life of the cell and the cell is biconvex. In mammals, the erythrocyte loses the nucleus during fetal life and the cell becomes biconcave, but nucleated erythrocytes may be seen under normal conditions in the marrow of bones, in the blood of the spleen and occasionally in the blood of the portal vein. The erythrocyte is a cell distinctively characteristic of craniata. In acranial vertebrates and in inverte-

* Presented before The Medical Society of the District of Columbia, May, 23, 1923.

brates all blood corpuscles are nucleated and the oxygen is carried by the hemoglobin within the blood serum. From the mesenchyme cells the hemohistoblasts develop and by their further structural differentiation they form the endothelial cells of the bloodvessels, the erythrocytes, leukocytes, blood platelets and lymphocytes. The part the reticulo-endothelial cells in the blood sinuses of the spleen play in the regeneration of the blood cells is not known, but in some of the diseases of the spleen many nucleated erythrocytes and myelocytes are found which is suggestive of active cellular regeneration within the spleen.

Historical Data. Splenic anemia is one of the diseases in which changes in the liver and blood accompanying splenomegalia have been studied. Gretsel, who was first to report a case of splenic anemia, described and published a case from the clinic of Professor Greisinger. Greisinger had recognized clinically splenic anemia, which up to his time had been included in a large group of splenomegalies of unknown etiology. Gretsel gives Greisinger credit for having used the term splenic anemia to distinguish it from other anemias with splenomegaly, which had hitherto been classified as pseudoleukemias. The next important publications are those of Banti who reported the clinical observations and autopsy studies of 3 cases, and made other contributions to the literature on the disease. The writings of Banti became well-known and splenic anemia is often called Banti's disease, but Banti gives to Gretsel the credit of describing, and to Greisinger the credit of recognizing and naming splenic anemia.

The original group called splenic anemia by Gretsel included what we now recognize as Gaucher's disease, hemolytic jaundice, von Jaksch's disease, tuberculosis of the spleen, luetic and malarial splenomegalies, and thrombophlebitis of the portal and splenic veins. These diseases have been eliminated from the original group because clinical and laboratory studies have proved them to be entities in themselves. The splenomegalies which we now classify as splenic anemias are characterized by an insidious onset; chronicity over a period of years, with crises; a gradual hypertrophy of the spleen, accompanied by a secondary anemia with leukopenia, and occasionally, during a crisis, intermittent fever with leukocytosis; a tendency to hemorrhage from the mucous membranes but mostly from the stomach; at times attacks of epigastric pain; increase in the size of the liver at the beginning of the disease but contraction later as cirrhosis develops; and, in the terminal stage of the disease, jaundice.

Etiology. When splenic anemia was described by Gretsel and later by Banti the term included a number of splenomegalies, the etiology of which was unknown. From time to time as clinical, pathological and etiological studies were made, certain splenomegalies with splenic anemia were removed from the original group,

and in our present group of splenic anemias no definite cause has been found. It is reasonable to presuppose this present group includes splenomegalies due to several different causes, and that we are now including several distinct clinical diseases or entities. By further studies, we may be able to determine the etiological factors of each, so as to differentiate the several varieties now included. Although the etiology is unknown, it is considered that the disease is primarily in the spleen. In some cases the history would suggest as the underlying cause, some metabolic derangement or faulty intestinal absorption, present since childhood. Banti and others considered it of infectious origin and the cause of those splenic anemias, in which the etiology has been determined, substantiates this view.

Malaria and some other fevers of infectious origin cause enlargement of the spleen during their course. This enlargement in some cases remains after the symptoms of the disease have disappeared. Any one of these infectious diseases which causes an enlarged spleen may be an etiological factor in splenic anemia. When the spleen is damaged and its function deranged, by an infectious disease, it may be susceptible to splenic anemia, whatever the cause may be.

Symptoms. Banti describes splenic anemia as "a disease characterized by a gradual progressive oligemia of unknown cause, which gives place to marked disturbance of all organic functions, to edema, hemorrhage, intermittent fever; followed almost always by death; accompanied by a conspicuous tumefaction of the spleen and very often of the liver, the tumefaction independent of any previous morbid state and not accompanied by leukemic change in the blood. Briefly, splenic anemia is a progressive idiopathic hypertrophy of the spleen and frequently of the liver, without leukemia." He divided the progress of the disease into three stages: (1) Gradual enlargement of the spleen with secondary anemia; (2) hypertrophy of the liver with diminution in the amount of urine; and (3) reduction in the size of the liver, and ascites.

In our present group we consider splenic anemia to be a disease of early adult life, which may have been present for a number of years, but owing to its insidious onset unrecognized until the prominent symptoms became manifest. It is a chronic disease, progressing over a period of years. Early in the disease the spleen begins to enlarge, the enlargement being huge in many instances. The hypertrophy is gradual. Accompanying the hypertrophy of the spleen there is a secondary anemia with leukopenia. The erythrocytes number about 2,000,000 to 3,000,000 per c.mm., the leukocytes about 4000 to 5000 and hemoglobin about 50 per cent. Following the hypertrophy of the spleen there is an increase and later a reduction in the size of the liver. With the increase in the size of the liver, the amount of urine is reduced, and as the liver contracts the diminution is even more marked and there is an accompanying ascites. In the course of the disease there are crises, during which there may

be epigastric pain and hemorrhage which may be slight, or enormous in amount and sufficient to cause death. Most of the bleeding is from the stomach, but it may be from other parts of the gastro-intestinal tract, or from the nose, kidneys and bladder, or there may be purpura. During a crisis there is intermittent fever, with leukocytosis. Late in the disease there is jaundice, the degree of which is dependent upon the damage to the liver. Beginning with the enlargement of the liver there is a gradual reduction in the amount of urine, with a marked diminution toward the terminal stage. The urine is high-colored and contains albumin and numerous casts.

Treatment. The recognized treatment of splenic anemia today is the administration of iron, transfusion and splenectomy. The administration of iron, either by mouth or subcutaneously, is of great value when the hemoglobin is lowered by the destruction of the erythrocytes or hemorrhage. Transfusion is a recent form of treatment and is an adjunct to the surgical treatment. Splenectomy for splenic anemia has been performed since the publications of Gretsel and Banti stimulated interest in this disease. Splenectomy had been performed before this time, and some of the earliest recorded cases of splenectomy might have been on cases of splenic anemia. Surgery of the spleen dates back to the Sixteenth Century. Splenectomy has been accredited by some authors to Zaccarelli in 1549 and to Ferrerius in 1711, but for lack of sufficient data these instances have not been accepted as authoritative. The earliest authentically reported cases of splenectomy are those of Quittenbaum of Rostock, in 1829, Kuchler of Dermstadt in 1855, and Spencer Wells of London in 1866. In each instance the patient died within a few hours following operation. In 1867 Pean did a successful splenectomy, from which the patient recovered. Collier's table, reporting 29 cases of splenectomy, covering a period from 1549 to 1881, shows a mortality rate of 72.4 per cent. Vanvert's thesis of 1897 gives a mortality rate of 37.9 per cent, recording 274 cases with 104 deaths. Mortality has since been reduced in splenectomy by proper selection of cases and employment of modern surgical technic. Giffin in 1921, in a series of 71 splenectomies for splenic anemia, reported only 9 deaths, a mortality rate of 12.6 per cent. The most favorable cases for splenectomy are those in which the spleen is only slightly enlarged, where only a moderate degree of secondary anemia exists, and where there has been no marked damage to the liver and other tissues. However, splenectomy has been done late in the disease, with favorable results, in cases which at first appeared hopeless. Lewis and Sweetzer have each reported a case of splenic anemia in which splenectomy was done late in the disease, following which the patient recovered. Having recently had under observation a patient who presented the characteristic clinical picture of splenic anemia, and in whom the disease progressed

to the third stage, and who was successfully treated by transfusion and splenectomy, we think this of sufficient importance to report in detail.

Case History. No. 1126.—Mr. V. B., a real estate broker, single, aged twenty-six years, was seen in consultation by me on January 28, 1922. There was no family history of disease of the blood or spleen. The patient gave a history of having had "liver trouble" at the age of seven years; typhoid fever at the age of eight; colitis at the age of fifteen and again at the age of seventeen. The present illness began seventeen years ago and has progressed steadily. He has had frequent digestive upsets which were considered "bilious spells," and was always inclined to be languid and drowsy. He took calomel and salts at frequent intervals. His symptoms were attributed to malaria, though this was not definitely established, as there were no chills, fever, or sweats, nor was the plasmodium found in the blood. At the age of seventeen years an enlarged spleen was first observed and since that time there has been a slowly progressive enlargement which has been accompanied by a gradually increasing secondary anemia. When the patient was twenty years of age, he had a hemorrhage from the bladder. In December 1917, at the age of twenty-one, he had a hemorrhage by mouth and in this same month he successfully passed the physical examination under enlistment in the Navy. His weight upon entering the Navy was 162 pounds. While in service in February, 1919, a hemorrhage by mouth occurred. On July 31, 1919, he was discharged from the Navy, his weight at this time being 196 pounds. At that time there was a very yellow cast to the skin and he was dark about the eyes. November, 1920, at the age of twenty-four years, he vomited a large amount of blood and passed tarry stools. Following this hemorrhage, blood examination on November 24, 1920, showed erythrocytes 2,190,000, leukocytes 20,800, hemoglobin 28 per cent. One week after this hemorrhage a diagnosis of duodenal ulcer was made, for which he was operated upon, elsewhere, on November 30, 1920, a gastroenterostomy being made. An omentopexy was also made on account of abdominal ascites. After the patient was operated upon, he improved, and was apparently in good condition. July 15, 1921, the erythrocytes numbered 5,500,000, leukocytes 7000 and the hemoglobin 80 per cent. In August, 1921, he had two roentgen-ray treatments over the splenic area of five and seven minutes duration, four days apart. Following this the patient became apparently worse and seemed exceedingly weak. On August 16, 1921, the erythrocytes numbered 4,300,000, leukocytes 6100, hemoglobin 82 per cent. Beginning on October 4, 1921, and continuing until October 8th, he had 11 hemorrhages. He bled from the mouth and rectum very profusely. On November 29 and 30, 1921, he again bled from the mouth and rectum (Table I).

TABLE I. HEMORRHAGES.

Date.	Age at time of hemorrhage.	Number of hemorrhages.	Location.
1916	20	1	Bladder.
Dec. 1917	21	1	Mouth.
Feb. 1919	23	1	Mouth.
Nov. 1920	24	1	Mouth and rectum (profuse).
Oct. 4, 1921	25	4	Mouth and rectum (profuse).
Oct. 5, 1921	25	3	Mouth and rectum (profuse).
Oct. 6, 1921	25	3	Mouth and rectum (profuse).
Oct. 8, 1921	25	1	Mouth and rectum (profuse).
Nov. 29, 1921	25	1	Mouth and rectum (profuse).
Nov. 30, 1921	25	1	Mouth and rectum (profuse).
Total		17	

During the gastroenterostomy operation on November 30, 1920, 2 gallons of fluid were taken from the peritoneum, and during the splenectomy operation on February 6, 1922, about the same amount was removed. From January 25, 1921 to March 16, 1922, the abdomen was tapped 46 times on account of abdominal ascites, withdrawing in all a total of 125⅜ gallons of ascitic fluid. With the amount removed at operation the total is 129⅜ gallons (Table II).

TABLE II. ABDOMINAL TAPPINGS.

Date.	Amount.	Date.	Amount.
Jan. 25, 1921	12 qts.	July 19, 1921	12¾ qts.
Feb. 8, 1921	13 "	July 27, 1921	13 "
Feb. 11, 1921	8 "	Aug. 3, 1921	12¾ "
Feb. 15, 1921	9 "	Aug. 10, 1921	12½ "
Feb. 21, 1921	8 "	Aug. 17, 1921	13½ "
March 2, 1921	14 "	Aug. 24, 1921	11½ "
March 9, 1921	13 "	Sept. 1, 1921	12 "
March 19, 1921	14 "	Sept. 8, 1921	12¼ "
March 26, 1921	13 "	Sept. 17, 1921	10 "
April 2, 1921	13 "	Sept. 26, 1921	9½ "
April 11, 1921	12 "	Oct. 14, 1921	7¾ "
April 21, 1921	12½ "	Nov. 7, 1921	6½ "
May 1, 1921	13½ "	Nov. 22, 1921	8½ "
May 11, 1921	14 "	Dec. 6, 1921	7 "
May 19, 1921	14½ "	Dec. 20, 1921	7½ "
May 26, 1921	14½ "	Dec. 28, 1921	7 "
June 2, 1921	13¾ "	Jan. 4, 1922	6¼ "
June 9, 1921	15¼ "	Jan. 12, 1922	5 "
June 16, 1921	14½ "	Jan. 21, 1922	5¾ "
June 23, 1921	16½ "	Jan. 28, 1922	6¾ "
June 30, 1921	16 "	Feb. 4, 1922	6⅛ "
July 1, 1921	12½ "	Feb. 17, 1922	2½ "
July 9, 1921	12¼ "	March 16, 1922	¼ "

Total Number of Tappings — 46.
Total Amount — 129⅜ gallons — (loss at operation estimated).

At the consultation on January 28, 1922, a splenectomy was decided upon, fully realizing that the condition of the patient made him a poor surgical risk.

Operation, February 6, 1922. The abdomen was opened through a high left rectus incision and upon exploration a moderately enlarged spleen was encountered. It was firmly adherent to the diaphragm, omentum, colon and stomach. With considerable difficulty the adhesions were separated and the spleen delivered through the abdominal incision. The pedicle was clamped, divided and ligated, and the spleen removed. Large hot packs were used to control the oozing from the under surface of the diaphragm. There was a large amount of ascitic fluid in the peritoneum. Exploration of the abdomen was difficult on account of numerous firm adhesions. The cecum could not be separated from adhesions holding it firmly in the right iliac fossa, and the appendix could not be brought into the operative field. The gall-bladder could not be palpated or inspected. The liver was small, hard and nodular and had the characteristic roughness of cirrhosis. As the spleen was being removed, Dr. Neuman transfused the patient with 500 cc of citrated blood (Table III).

TABLE III. TRANSFUSIONS

Date.	Amount.	Method.	Donor.	Reaction.
Oct. 5, 1921 . . .	650 cc	Direct	Brother	None.
Oct. 28, 1921 . . .	450 cc	Direct	Brother	None.
Nov. 14, 1921 . . .	600 cc	Direct	Friend	Fever, four days.
Feb. 6, 1922 . . .	500 cc	Indirect (citrate)	Friend	None.

Pathological Report. Weight of spleen 790 gm; it measures 19.5 cm. in length and 13 cm. in width. The superior surface is covered with a thick yellowish fibrinous exudate which is rough and torn in many places. The under surface in the region of the hilum is a dark lavender color. The organ sectioned with resistance. On section the surface is a dark purplish color with numerous trabeculations and thickened bloodvessels. The capsule is thickened and measures 3 mm. The exudate on the capsule measures 0.5 cm. (Fig. 1).

Microscopical Examination. The capsule is markedly thickened and is made up of a dense fibrous tissue. Over the surface of the capsule there is a fibrinous exudate throughout which there are numerous small round cells. In all the fields studied there is a marked fibrosis and the trabeculæ are thickened. Only an occasional Malpighian body can be found and these show replacement with fibrous tissue (Figs. 2, 3, 4).

FIG. 1.—(Case 1126.) Photograph of the superior surface of spleen, showing a marked perisplenitis.

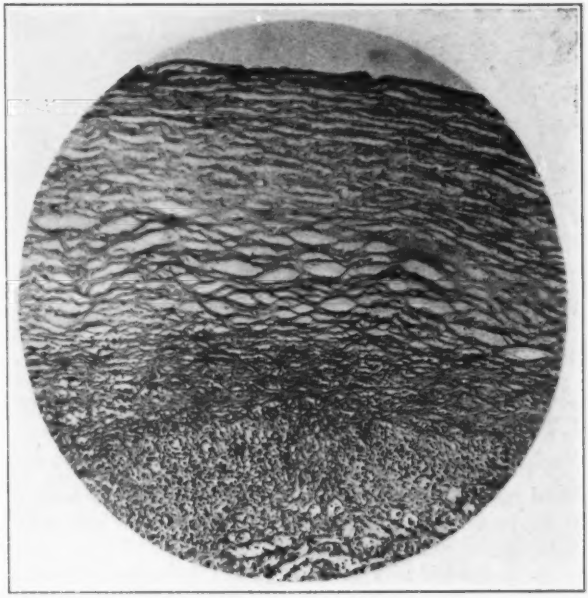


FIG. 2.—(Case 1126.) Photomicrograph of section of spleen, showing thickened capsule and fibrinous exudate on capsule. The exudate on capsule is made up of dense fibrous tissue, in which there is marked hyalinized fibrosis. The capsule is markedly thickened and is made up of a dense fibrous tissue, in which there is an infiltration of small round cells.

Pathological Diagnosis. Chronic splenitis.

Convalescence. For a few weeks after the operation there was a small amount of ascitic fluid in the abdomen, which soon ceased to accumulate. The convalescence was marked by bronchopneumonia, cystitis and separation of the wound. The bronchopneumonia and cystitis responded to treatment and the wound was resutured under local anesthesia. From this point convalescence was slow. The patient was weak and confined to his bed until the early part of April, when he was placed in a chair for a short time each day. After he was well enough to sit up, his appetite improved and an increase of strength was noted.

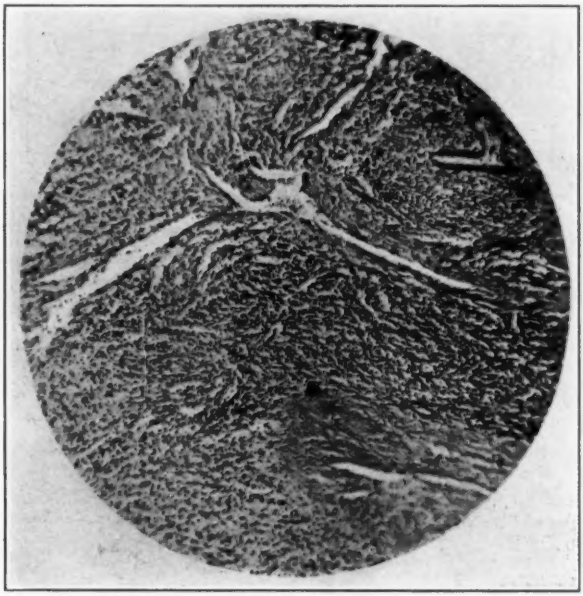


FIG. 3.—(Case 1126.) Photomicrograph of section of spleen, showing thickening of the trabeculæ, marked increase in the fibrous tissue of the bloodvessels and fibrosis throughout the reticulum. The cells of the splenic pulp are made of lymphocytes, leukocytes and red blood cells, but are not numerous.

He continued to do well until the latter part of May, when he developed pain in the lower right quadrant of his abdomen, accompanied by tenderness and rigidity on pressure. There was a rise of temperature and nausea and vomiting. These symptoms became more marked and on June 2, 1922, a diagnosis of abdominal abscess was made, for which he was operated upon.

Operation, June 2, 1922. Under nitrous oxide-oxygen anesthesia, a split muscle incision over McBurney's point revealed a large

abdominal abscess, probably caused by an appendicitis, filling the lower right quadrant of the abdomen and the pelvis with thick pus. The abscess was evacuated of pus and drainage established. This abdominal abscess delayed convalescence considerably. It was not until about one month later that the patient could be gotten up in a chair again. After he was well enough to get up again his appetite improved, strength returned, and there was a gradual progressive improvement in his condition, so that by the end of the summer he was well enough to walk about a little.

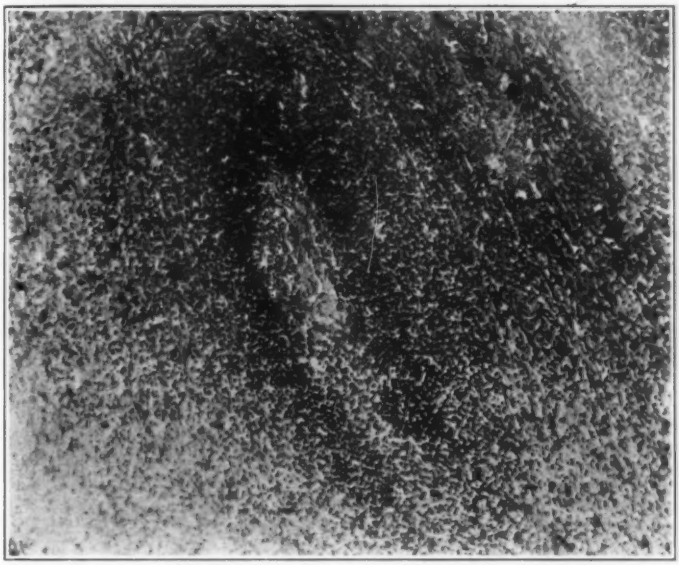


FIG. 4.—(Case 1126.) Photomicrograph of section of spleen, showing germ center, the central portion of which is made up of dense fibrous connective tissue which has contracted. There is a marked diminution of lymphoid cells.

On the evening of September 27, the patient became nauseated a few hours after supper and vomited. During the night an enema was given, but it was not very effective. The following day the nausea continued and the results of an enema were unsatisfactory. On September 29, 1922, the patient had fecal vomiting, the abdomen was distended, there had been no bowel movement, and a purgative enema, given at that time, was returned clear. A diagnosis of intestinal obstruction was made, for which immediate operation was advised.

Operation, September 29, 1922. The abdomen was opened through a low right rectus incision and exploration through it was made with some difficulty, on account of numerous adhesions. The

wall of the abdominal abscess, the upper part of which was formed by the terminal ileum, and omentum had contracted, producing several acute angulations of the ileum, which caused the obstruction. Part of the tissue forming the abscess wall was removed and the obstruction relieved by dissecting the ileum from its attachments. Following this operation the patient has continued to improve steadily. There has been a marked increase in strength, the weight gain has been over 80 pounds and his general condition is very good. On February 10, 1923, a cytological study of the blood showed erythrocytes 4,700,000, leukocytes 7000 and hemoglobin 90 per cent (Table IV).

TABLE IV. BLOOD COUNTS.

Date.	Hemoglobin.	Red blood corpuscles.	White blood corpuscles
Nov. 24, 1920	28	2,190,000	20,800
Nov. 25, 1920	33	2,240,000	
Nov. 26, 1920	32	2,320,000	
Nov. 27, 1920	31	2,190,000	
Nov. 28, 1920	35	2,310,000	
Nov. 29, 1920	38	2,620,000	
Feb. 1, 1921	55	3,500,000	5600
March 11, 1921	64	3,500,000	7600
June 15, 1921	80	5,550,000	7000
Aug. 16, 1921	82	4,300,000	6100
Oct. 1, 1921	68	4,536,000	7160
Oct. 4, 1921	60		
Oct. 24, 1921	33	1,784,000	8280
Nov. 13, 1921	33	2,896,000	8200
Nov. 18, 1921	75	3,430,000	7360
Nov. 25, 1921	60	3,000,000	5440
Dec. 7, 1921	55	2,550,000	7700
Jan. 16, 1922	31	3,370,000	5700
Jan. 24, 1922	50	2,980,000	4000
Feb. 6, 1922	Splenectomy		
Feb. 7, 1922	..	.....	27,000
Aug. 21, 1922	75	3,500,000	9000
Feb. 10, 1923	90	4,700,000	7000

Conclusions. 1. Diseases of the spleen are uncommon and are often missed. In the case reported by Lewis and in this case, following vomiting of blood, a diagnosis of ulcer was made and a gastroenterostomy was done.

2. When a patient has a gastro-intestinal hemorrhage with epigastric pain, the spleen and blood should be studied.

3. The case of Lewis, that of Sweetzer, and the case reported here, demonstrate that a patient in a late stage of splenic anemia may be successfully splenectomized if he has had proper preparation by medical treatment and transfusion.

4. In the preoperative preparation, at the time of operation, and later, transfusion should be done as indicated.

5. Splenectomy should not be done in splenic anemia without considering the risk due to secondary anemia and damage to the liver and other tissues.

6. The recovery of this case helps to strengthen the view that whatever the cause of splenic anemia may be, it is primarily in the spleen.

BIBLIOGRAPHY.

Banti, G.: Dell' Anemia Splenica, Archivio della Scuola D'Anatomia Patologica, Firenze, 1883, **2**, 53.

Collier, H.: Splenectomy: A Justifiable Operation in Leukocythemia (?), Lancet, 1882, **1**, 219.

Ferrerius: Quoted by Banti.

Giffin, H. Z.: The Present Status of Splenectomy as a Therapeutic Measure, Minnesota Medicine, 1921, **4**, 132.

Gretsel: Ein Fall von Anemia Splenica bei einem Kinde, Berl. klin. Wchnschr., May 14, 1866, p. 212.

Griesinger: Quoted by Banti.

Kuchler: Quoted by Banti.

Lewis, M. J.: Splenic Anemia, Splenectomy and Recovery, Am. Jour. Med. Sci., 1908, **136**, 157.

Pean: Quoted by Banti.

Quittenbaum: Quoted by Banti.

Sweetzer, H. B.: Splenectomy in Third Stage, Banti's Disease, Surg. Gynec. and Obst., 1921, **33**, 376.

Vanverts, J.: Thèse pour le Doctorat en Medecine de la Splenectomie, 101, Paris Thesis, 1897.

Wells, Sir T. S.: On Excision of Enlarged Spleen with a Case in Which the Operation was Performed, Med. Times and Gaz., 1866, **1**, 2.

Zaccarelli: Quoted by Banti.

COMBINED SCLEROSIS OF THE SPINAL CORD AND CARCINOMA OF THE STOMACH.

REPORT OF A CASE.

By John L. Garvey, M.D.,

and

Louis D. Stern, M.D.,

ann arbor, michigan.

(From the Departments of Neurology and Internal Medicine, University of Michigan Medical School.)

Cases of combined degeneration of the spinal cord associated with carcinoma of the stomach and simulating pernicious anemia are sufficiently rare in the literature to warrant reporting. Hurst, commenting on a case of this type reported by Waterfield and Shackle,[1] states that he and Bell[2] failed to discover any record of an actual case of cancer of the stomach with subacute combined degeneration of the cord. Several writers, however, have referred to the possible occurrence of such an association as an alternative

to the more common one in Addison's anemia. Hurst and Bell advance the opinion that the achlorhydria of pernicious anemia, with or without subacute combined degeneration of the cord, is not the result of any specific gastric disease, as it might ensue from a variety of causes; and there is no reason why cancer of the stomach should not be one of these.

Case Report. An adult male, aged fifty years and a janitor by occupation, entered the Clinic for Neurology of the University Hospital, November 21, 1922, complaining of numbness and tingling in the hands and feet. His father had died of cancer. He had never married, insisted he had had no previous serious illness and denied venereal disease. His present illness was of rather short duration. About a month previous to entrance he noticed that his hands and feet would become swollen following heavy work, and shortly after this he experienced numbness and tingling in the extremities. These symptoms progressed and he soon found that he could not ride a bicycle which he had been in the habit of doing. He had no other complaints referable to the gastrointestinal, cardiovascular or nervous system.

Examination showed that he was only fairly well nourished and he appeared about his actual age. He seemed mentally normal and of about average intelligence. There was a definite lemon-yellow color to the skin, and the scleræ were china blue. The tongue was smoothed out and tremulous. The pupillary reflexes were somewhat slow. There were no extraocular palsies and no nystagmus, and the function of the other cranial nerves was normal. He wore an upper plate and the few remaining teeth showed some caries. The right hand was somewhat puffy. The tendon reflexes were all present, prompt and equal. There was a marked spinal ataxia on the finger-to-nose test, and his gait was of the bilateral spastic ataxic type. Sense of motion and position was lost in the toes, and deep muscle sense was lost in the ankles. Vibratory sense was normal. The plantar reflex at this time was flexion. Both eyes showed early lenticular changes and the fundus was of the arteriosclerotic type. Examination of the heart, lungs and viscera of the abdominal cavity was entirely negative. Blood-pressure was 105/70. The urine examination was negative. The Wassermann test on the blood and spinal fluid was negative, and the spinal fluid was normal to other chemical and serological tests. Examination of the blood at this time showed hemoglobin 81 per cent, red blood cells 3,150,000, white blood cells 5100 with a normal differential white cell picture and no noteworthy changes in the red cells indicative of pernicious anemia.

In view of the association of a combined degeneration of the spinal cord, an anemia and a lemon-yellow color of the skin it seemed reasonable to assume that this was a syndrome of rather common occurrence. Woltman[3] believes that this type of cord involvement

with an anemia which does not show the characteristics of the pernicious type is nevertheless potentially of that type; and the literature is quite full of reports of cases of posterolateral sclerosis which eventually develop the classical picture of pernicious anemia. Moreover, the case here presented did show one of the most characteristic blood findings of Addisonian anemia; namely, a high color index. The diagnosis of that disease therefore was strongly entertained.

Low-power photomicrograph of the spinal cord, from the authors' case, showing sclerosis of the type and distribution associated with pernicious anemia. (Courtesy of Professors Warthin and Weller.)

Repeated blood examinations over a period of several weeks with the expectation of showing some significant change, revealed no further evidence of primary blood disturbance, although the anemia progressed and the hemoglobin decreased to 60 per cent. Gastric analysis showed absence of free hydrochloric acid and very low total acidity. Examination of the stool was entirely negative.

After about six weeks in the hospital the patient began to complain of slight gastric disturbance after eating, not amounting to pain. He noted a feeling of fullness, which he attempted to relieve by induced emesis. The vomited material after a meal was excessively large in amount and contained numerous yeasts and Oppler-Boas bacilli, no free hydrochloric acid, no blood. Gastrointestinal roentgen-ray at this time revealed a permanent prepyloric defect, typical of gastric carcinoma. In view of the evidence of pyloric obstruction, operation was advised and posterior gastroenterostomy

was done. The surgeon noted extensive carcinoma with lymph gland metastases, and incidentally an apparently normal spleen and liver.

Recovery from the operation was uneventful, and for a time there was relief from the gastric symptoms. About six weeks later, however, it was seen that the patient was losing weight with the return of vomiting and the onset of epigastric pain, which had not been present before. During the ensuing month he became progressively worse in every respect. The knee and ankle reflexes became exaggerated and later were entirely lost, with a complete paralysis of the lower extremities and retention of urine. On May 19, 1923, six months after admission to the hospital, he died.

Autopsy Findings. The spinal cord showed marked posterolateral degeneration of the type seen in pernicious anemia, more marked in the dorsal than in the cervical region. A diffusely infiltrating adenocarcinoma was found to involve the pyloric end of the stomach, with metastases in the peritoneum and mesenteric lymph nodes but with none in the cord or bone marrow. The bone marrow was hyperplastic. The liver and spleen showed only chronic passive congestion and atrophy, without malignant metastases and without any increased deposition of iron.

Discussion. The clinical and pathological findings definitely established the coexistence here of combined sclerosis of the spinal cord and carcinoma of the stomach. The question of primary interest concerns the possibility of an accompanying pernicious anemia of which the cord lesion may be a part. If, as has been argued by Woltman[3] and others[2, 4, 5], the presence of combined sclerosis with an anemia of any type is sufficient for a diagnosis of pernicious anemia, then that disease is certainly not to be easily eliminated in this case. Carcinoma of the stomach has been noted in the presence of undoubted pernicious anemia[6] although the signs and symptoms leading to such diagnoses are often to be explained on the basis of the cancer alone. For this reason much of the clinical data bearing on the question is useless. It is conceivable that the case under discussion would eventually have developed typical pernicious anemia had the cancer not killed him, but this involves the assumption that death was due primarily to the carcinoma which may not have been the case. Indeed, from the clinical standpoint, the signs of spinal cord degeneration progressed about as rapidly toward the termination of the case as did those of the cancer, and may have contributed just as much toward determining the outcome.

The most important single diagnostic feature of pernicious anemia is naturally the change in the blood, and one of the most characteristic details of this change is the high color index. This alone, among all the special features to be expected, was found in this case, and there was no marked fluctuation in the blood picture

at any time. In view of the well established fact that uncomplicated cancer of the stomach may produce this sign, no weight can be placed upon it as favoring the existence of a primary blood disturbance.

The sclerosing glossitis so commonly seen in pernicious anemia, which was noted in this case, is not necessarily indicative of that disease, for it may unquestionably be encountered under other conditions; and every case of true Addisonian anemia does not always show it. While it is an undoubted aid in diagnosis, there is no definite reason for considering it a specific sign of any greater value than the achlorhydria, to which it may be closely related. Just as the absence of free hydrochloric acid in the stomach may be due to a variety of causes, notably to cancer, so the glossitis may, under unusual conditions, be due to other agents. As an example of the occasionally misleading and unusual combination of signs, it may be stated that the writers have recently observed a case of disseminated sclerosis with achlorhydria, which came to autopsy, and in which the cord lesions were so distributed as to give rise to signs which simulated closely the typical findings of combined sclerosis.

The possible etiologic relationship of achlorhydria to combined sclerosis of the cord has been pointed out particularly by Hurst and Bell[2] and Vanderhoof.[7] From this point of view it is possible to consider the foregoing case as one primarily of cancer of the stomach, with the cord lesions developing as a result of the deficient gastric secretion. The history of the case lends some color to this conception because the symptoms of the spinal cord degeneration were of relatively short duration, and antedated the onset of definite gastric disturbance by only ten weeks. Moreover, the progress of the case indicates that both the carcinoma and the posterolateral sclerosis developed rapidly and coincidently, in such a way as to make it very difficult, if not impossible, to decide which pathological process contributed more toward determining the final outcome. This idea is purely theoretical, however, for combined sclerosis of the spinal cord has never been noted as a true complication of gastric cancer in any of the innumerable cases of that disease on record.

From the pathological standpoint, the presence or absence of true pernicious anemia in this case cannot be definitely determined. The hyperplastic bone marrow is suggestive, but far from conclusive. The hemosiderosis of various organs, particularly of the liver, spleen and kidneys, which has been stressed by the older writers as being so characteristic of pernicious anemia, is not an invariable finding at autopsy. Absence of it, therefore, does not eliminate the disease.

The question as to whether or not pernicious anemia was present in the foregoing case cannot be definitely answered. The diagnosis

may or may not be made according to the criteria of various competent observers. On the basis of the general diagnostic rule that signs and symptoms are to be explained by the simplest plausible diagnosis, it would seem that the presence of pernicious anemia is not necessary to explain the findings. While it is probably true that the majority of cases presenting a combined sclerosis of the spinal cord and an anemia will eventually show the changes found in pernicious anemia, it must nevertheless be borne in mind that this general rule will have its exceptions. In the diagnosis of any particular case, certain details of the examination may be found to assume unexpected importance and may materially alter not only the clinical interpretation, but the prognosis and treatment as well.

Summary. 1. A case of combined sclerosis of the spinal cord and carcinoma of the stomach, with autopsy findings, is reported.

2. The close resemblance clinically and pathologically between this combination of diseases and that including pernicious anemia is pointed out.

3. The importance prognostically and therapeutically of determining the etiology of an accompanying anemia in cases of combined degeneration of the spinal cord is emphasized.

REFERENCES.

1. Waterfield, R. L., and Shackle, J. W.: Guy's Hospital Reports, 1923, **73**, 208.
2. Hurst, A. F., and Bell, J. R.: Brain, 1922, **45**, 266.
3. Woltman, H. W.: Collected Papers of the Mayo Clinic, 1918, **10**, 933.
4. Hurst, A. F.: Brit. Med. Jour., 1924, **1**, 93.
5. Bramwell, B.: Brit. Med. Jour., 1910, **1**, 1396.
6. Brandes, T.: Med. Klinik, 1921, **17**, 189.
7. Vanderhoof, D.: Arch. Int. Med., 1923, **32**, 958.

THE TREATMENT OF TETANUS, WITH SPECIAL REFERENCE TO THE USE OF MAGNESIUM SULPHATE.

By Carroll Smith, M.D., F.A.C.S.,

PROFESSOR OF SURGERY, ST. LOUIS UNIVERSITY, SCHOOL OF MEDICINE,

AND

W. E. Leighton, M.D., F.A.C.S.,

PROFESSOR OF SURGERY, ST. LOUIS UNIVERSITY, SCHOOL OF MEDICINE, ST. LOUIS, MO.

(From the Department of Surgery, St. Louis University, School of Medicine.)

While great advances have been made in our knowledge of tetanus since the discovery of the "bacillus of earth," by Nicolaier[1] in 1884, and the isolation of the tetanus bacillus, by Kitasato[2] in 1889, and the introduction of tetanus antitoxin, by Behring and

Kitasato[3] in 1890, nothing has been found which will overcome the strong combination between tetanus toxin and nerve tissue. We must admit that the treatment of tetanus still is prophylactic and symptomatic.

The prophylactic value of antitoxin in tetanus is so evident that any fair-minded man should be convinced, and it is not necessary to produce the numerous statistical reports and experimental evidences which prove this assertion. It is true that tetanus antitoxin does not always prevent the development of tetanus, but the prophylaxis is successful in the great majority of cases, when the serum is properly administered. Tetanus may develop after prophylactic serum according to Donati[4] as follows:

1. Mild tetanus after a long incubation period.
2. Local or partial tetanus.
3. Fulminating tetanus, with a very short incubation period.

Kuemmell[5] states that a small number of individuals are so very susceptible to tetanus toxin that the antitoxin fails to function. Tulloch[6] points out that there are at least three different strains of toxic and more than one non-toxic strain of tetanus bacilli, and this may account for the failure of prophylactic antitoxin at times. To these types should be added late and recurrent tetanus. Ashhurst[7] states that the prophylactic effects of the serum disappear between eight and ten days, so that dormant bacilli or spores may become active after that period, and produce typical symptoms. Speed[8] has called attention to recurring tetanus, and reports a case recurring seventeen months after the original attack. Recurring tetanus after serum usually follows the retention of a foreign body. This was the condition in Speed's case and similar cases are reported by Stauff,[9] Bungart[10] and others. Vernoni[11] mentions 4 cases, apparently cured of tetanus, in which new attacks were aroused by trauma or operations. Montois[12] and Courtois-Suffit[13] state that dormant spores may be awakened months after implantation. Kuemmell[5] and Courtois-Suffit[13] emphasize the importance of giving tetanus antitoxin just before operation, performed after a recent attack of tetanus or a recent suspicious wound. Courtois-Suffit[13] and Gessner[14] advise repetition of the prophylactic serum in seven to ten days in the presence of suppuration. Bruce[55] advises that the primary injection of prophylactic serum be followed by secondary and further prophylactic doses, as long as the wound remains suspicious.

While 1500 units of serum given at once, and repeated in ten days, generally is used, Ochsner[15] advises ten times this dose. Chavasse[16] states that the prophylactic dose of serum should be in proportion to the gravity of the wound, and that it should be increased especially in the presence of a foreign body.

It was found early that tetanus antitoxin would not cure tetanus after the symptoms were present, due to the firm combination of

the toxin with nerve tissue. It also was recognized early that sedatives were needed in the treatment, as it was realized that death was due to exhaustion, starvation or asphyxia during a spasm, and not directly to the toxin. Many sedatives have been advised, such as morphin, chloral, chloretone, by Hutchings;[17] persulphate of soda by Bérard and Lumière;[18] Du Bouchet,[19] a preparation of curare called curaril; by Bergell and Levy,[20] spinal injections of morphin and eucain by Murphy;[21] intravenous ether-salt solution by Hercher,[22] and later luminal. All these preparations did not meet expectations.

In 1899 Meltzer[23] first noticed that the effect of magnesium salts was inhibitory when given intracerebrally in rabbits. In 1905 Meltzer and Auer[24] studied experimentally the effects of magnesium salts on numerous animals, and they found that the effect always was inhibitory and no stimulating action was ever seen. In later experiments they[25, 26] studied the effects of magnesium salts when given intravenously, intramuscularly and intraspinally, and they found in each case that the effect always was inhibitory and tended to produce paralysis.

Meltzer and Auer[27] then studied the effects of magnesium sulphate in the treatment of tetanus in monkeys and found that it had marked influence in controlling the spasms in these animals. Acting on these findings of Meltzer and Auer, Blake[28] treated the first case of human tetanus in a boy by magnesium sulphate in 1906. He used intraspinal injections of magnesium sulphate and succeeded in curing a very severe case of tetanus. Other early, successful cases were reported by Logan,[29] Miller,[30] Hessert,[31] Kocher,[32] Robertson[33] and others.

There is no question that the use of magnesium sulphate is the greatest advance in years in the treatment of tetanus. The effect is purely symptomatic. It acts to prevent death from exhaustion or asphyxia, until the patient is able to eliminate the toxin which is in combination with nerve tissue. The effect comes on very soon after the injection. Under appropriate application the patient becomes quiet, the spasms become less, or disappear, and the spastic muscles relax. The patient takes nourishment, is comfortable and sleeps. Straub[34] noted that magnesium sulphate relaxed spastic muscles before affecting normal muscle function.

Magnesium sulphate may be administered by four routes: Subcutaneous, intramuscular, intravenous and intraspinal. A 25 per cent solution of chemically-pure crystalline magnesium sulphate should be used in all methods, except the intravenous, where a 6 per cent solution is employed. The solution should be sterilized by boiling, or in the autoclave.

Weston and Howard,[56] who recently have reported excellent results in using magnesium sulphate, subcutaneously and intramuscularly, as a sedative in patients suffering from psychic dis-

turbances, advise that crude magnesium sulphate should be recrystallized three times, in order to secure a pure product. In the *subcutaneous method* 1.2 to 2 cc of a 25 per cent solution to each 20 pounds of body weight should be used four times in twenty-four hours. In severe cases 16 cc of the solution should be used four times in a day. The treatment should be repeated until all symptoms have disappeared. By this route the action is slower, but it is cumulative. It is the least dangerous method, but it may not suffice in very severe spasms unless large doses are given. *In intramuscular administration* Meltzer[35] advised that the patient be anesthetized by ether, then 2 cc of a 25 per cent solution to each 20 pounds of body weight should be injected into the muscles. This method may bring relief in less than half an hour and the effect lasts for two or three hours. The drug is more toxic by this method, and it should not be employed as a routine measure, but withheld for severe spasms. The *intravenous method* gives a more prompt effect than any other method, but its action may disappear in thirty minutes. This is a dangerous method, as the myocardium may be affected if the drug is injected too rapidly and respiratory paralysis is then prone to occur. It should be used only in great emergency, such as spasm of the diaphragm or larynx, where quick action is demanded, and means, as mentioned below, for treating the serious effects should be at hand. By this method Meltzer[36] advises a 6 per cent solution of magnesium sulphate given at the rate of 2 to 3 cc per minute and stopped as soon as there is beginning relaxation, or when serious heart or respiratory symptoms appear. These untoward effects disappear rapidly after the injection is stopped. When used by the *intraspinal method* the effect usually is manifested in less than a half hour and complete relaxation is present within one hour. The relief is longest by this method and lasts from twelve to thirty hours. Ether anesthesia frequently is required to carry out this method, especially if opisthotonos is present. One cubic centimeter of a 25 per cent solution of magnesium sulphate should be injected to each 20 pounds of body weight. The second dose should be smaller, about 0.8 cc to each 20 pounds of body weight. Only 0.5 cc of a 25 per cent solution to each 20 pounds of body weight should be used in a child. However, Meltzer[36] quotes that Kocher advises against the use of magnesium sulphate as a routine in children. The doses advised above are merely suggestive and are given as a working basis. The dosage should be decreased or increased until the desired effect is produced, that is, the relief of exhausting spasms. Magnesium sulphate should never be given in sufficient amount to completely relax the patient. It should be stopped when the relaxation is sufficient to permit feeding and to bring rest and comfort to the patient.

The only serious danger in the employment of magnesium sul-

phate seems to be the danger of respiratory paralysis. This effect may be relieved by calcium chlorid which reverses the action of the magnesium sulphate and brings back the tetanic spasms. A 2.5 per cent solution of neutral calcium chlorid in normal saline should be given slowly, intravenously, until the respiration is improved. The effect usually is seen within thirty seconds.

Ten to 15 cc of a 2.5 per cent solution of calcium chlorid given *intramuscularly*, and repeated if necessary, may slowly neutralize the unfavorable respiratory effect of the magnesium sulphate without causing the spasms to recur, and this method is advisable in less severe conditions. Joseph and Meltzer[37] have found that physostigmin in 1 mg. doses is sufficient in combating this respiratory depression. Artificial respiration, especially the intratracheal insufflation of Meltzer and Auer may be necessary. In respiratory failure following the intraspinal use of magnesium sulphate calcium chlorid does not act to overcome the complication, and Meltzer[35] advised that the spinal canal be washed out with Ringer's solution or with normal saline solution. Meltzer and Lucas[38] have shown that magnesium salts are eliminated to a great extent through the kidneys. The use of magnesium sulphate may cause urinary retention by paralysis of the muscles, according to Kocher[32] and others. Hyaline casts may appear in the urine. (Peck[39] and Gates.[40]) These complications disappear early and are temporary. The intravenous injection of magnesium sulphate produces considerable hyperglycemia with a mild glucosuria. This, however, is a temporary effect, and is no contraindication to the use of magnesium salts. (Meltzer.[36])

Meltzer[35, 36] advised the employment of magnesium sulphate in the treatment of tetanus as follows:

1. The subcutaneous method every six hours, as a routine.
2. If severe spasms, employ the intraspinal method and repeat if needed.
3. If an element of immediate danger, use the intravenous method.
4. If the intraspinal or intravenous methods are not practical, give intramuscular magnesium sulphate with ether anesthesia.

The magnesium sulphate should be used boldly, but one should be ready to combat the complications. These complications cannot be considered as serious objections to the use of magnesium sulphate, as we are dealing with a very dangerous and fatal disease, and heroic methods must be employed. Furthermore, the serious complications can be combated in this method, better than when other sedatives are used. Kocher,[32] after great experience with the use of magnesium sulphate in tetanus, is enthusiastic in advising its use. Robertson[33] recommends the method highly, and says "there is no such array of evidences for any other sedative." Pribam,[41] in October, 1916, reviewed 148 articles in the Teutonic literature, and concluded that magnesium sulphate is the best

palliative for the treatment of tetanus. Buzello[51] states that magnesium sulphate is the best remedy to alleviate spasms and the general reflex excitability.

Magnesium sulphate should not replace the use of tetanus antitoxin. As has been previously stated, there is no evidence that magnesium sulphate has any effect on tetanus toxin, either free or combined. Furthermore, it generally is accepted that antitoxin has very little, if any effect, on toxin combined with nerve tissue. However, it is very important to give tetanus antitoxin freely and early, in order to neutralize the toxin in the circulation, and at the site of origin and to prevent further combination of the free toxin with nerve tissue, for the toxin does not produce tetanic symptoms when circulating in the blood, and acts only when it reaches the nerve cells. Thus the antitoxin acts to prevent the further progress of symptoms, and stops the further attack of the toxin on the nerve cells. The antitoxin may be given by the subcutaneous, intravenous, intraspinal or the intramuscular route. Park and Nicoll[42] are ardent advocates of intraspinal serum, and report better results by this method. However, they also use serum intravenously and sedatives. Ashhurst,[7] Bruce,[44] Andrews[45] and Golla[46] also favor the intraspinal method. Stone[47] recommends the use of serum in tetanus as follows: First day, 20,000 units, intravenously (20,000 units, intraspinally); second and third days, 20,000 units, intravenously (20,000 units, intraspinally); eighth or ninth day, 10,000 units, subcutaneously or intramuscularly; a total of about 125,000 units in adults. The use of serum lessens the mortality mainly by stopping the supply of toxin to the nerve tissue. As the intraspinal method generally requires anesthesia, it probably is better to try the subcutaneous and intravenous methods of administering the serum first. If the patient is getting worse or the condition is desperate serum should be used at once by the intraspinal route.

Anaphylactic shock may occur after the use of tetanus antitoxin, but death from this complication is unknown according to Ashhurst.[7] Stone[47] quotes that the British war statistics report that it occurs in 2 per cent of intraspinal injections, in 6 per cent of intravenous and in 0.2 per cent of subcutaneous injections. Ten minims of epinephrin chlorid usually relieve the symptoms of anaphylaxis. Serum rashes occur in 40 to 50 per cent of the cases. Calcium lactate, $\frac{3}{4}$ gr., given intravenously, usually relieves the condition.

In addition to the use of serum and sedatives, the local treatment of the wound is very important. The wound should be opened and foreign bodies should be removed. Aërobic conditions should be maintained. Balsam of Peru locally applied to the wound has been ardently advised by Kreuter[48] and Ritter.[59] As shown by Ashhurst[7] and Vaillard,[49] symbiosis with other bacteria, and other factors are necessary for the production of toxin by the tetanus

bacillus or tetanus spores. Speed[50] states that pure tetanus spores, free from toxin, injected into an animal are harmless in the absence of toxin, and the spores are devoured by the leukocytes. Anything which acts to prevent the leukocytes from getting to the spores permits the toxin to be developed and to produce symptoms. Secondary infection, necrotic tissue, blood clots and foreign bodies, all favor the development of toxins, interfere with the action of the leukocytes and supply anaërobic conditions.

Tincture of iodin not only acts as an excellent preventive of secondary infection, but seems to have some specific effect against tetanus toxin locally. MacConkey and Zilva[51] and Teale and Embleton[52] have showed that iodin mixed with tetanus toxin lessened the effect of the toxin. Kuemmell[53] states that tincture of iodin applied to wounds almost always prevented the development of tetanus in veterinary practice. Ashhurst[7] and Tullidge[54] also emphasize this value of tincture of iodin. The well-known efficacy of iodin in preventing infection in accidental wounds and the apparent neutralizing effect of the iodin on tetanus toxin seems to indicate that its use locally is based on sound reasoning. As it is well established that tetanus toxin travels up the peripheral nerves, it seems rational to inject 5000 units of antitoxin about the wound of origin of the tetanus, with the idea of blocking the toxin.

In this connection, we desire to present 8 recent consecutive cases of acute tetanus, all of which recovered under treatment with magnesium sulphate and antitetanic serum.

Case Reports (by Dr. Smith). CASE I.—Mrs. L. L., aged sixty-eight years, was sent to the Lutheran Hospital by Dr. Reinhold Speer, June 25, 1922. She gave a history that her jaw became locked four days before admission. She had spasms in her throat and could not swallow. The patient had an abscessed tooth about three days before the symptoms began, and presented a complete prolapse of the uterus, with ulceration of the parts. The incubation period was not definite, as the point of origin was uncertain. On admission, the patient had extreme trismus, with rigidity in the neck and legs. The recti muscles were so rigid that they felt like steel plates. The temperature was 99.4° F. and the pulse was 120. She had not been able to take food or drink for several days. The patient was given 3000 units of antitoxin and 30 gr. of chloral hydrate at once. Ten thousand units of antitoxin were given intravenously and 16 cc of a 25 per cent solution of magnesium sulphate were given every five hours. On the next day, June 26, the condition was much improved. The spasms in the jaws, legs and recti muscles were distinctly lessened. The patient could take food and water, and had slept fairly well during the night. On the next day, June 27, the patient could open her jaws fairly well, and was

quite comfortable and free from spasms. Twenty thousand units of antitoxin were given. On the following day, June 28, three days after admission, the magnesium-sulphate injections were stopped, as considerable local irritation was occasioned by the injections. The next day, June 29, the muscles were again quite rigid and painful, so that the magnesium-sulphate injections again were employed and 20,000 units of antitoxin were given intravenously. After a few hours the patient was sleeping, and her condition was decidedly improved. On June 30 the injections of magnesium sulphate were stopped again. The rigidity increased somewhat, but was relieved by the further employment of magnesium sulphate. On July 3, eight days after admission, 1500 units of antitoxin were given subcutaneously. The patient returned home, July 9, entirely relieved.

Comment. This was a very severe case of tetanus in an old woman. Her condition had been getting worse daily. She received a total of 54,500 units of antitetanic serum. On three different occasions the spasms recurred after the magnesium sulphate had been discontinued, and each time the spasms were relieved again by injecting magnesium sulphate. The effect was so convincing that I feel certain that the recovery was largely due to the effect of the magnesium sulphate.

CASE II.—H. F. W., a male, aged thirty-five years, was referred to me by Dr. C. R. Hawker at the Alexian Brothers' Hospital, November 12, 1922. Nine days before, a drill passed through his left thumb while he was drilling an old mudguard of a motorcycle. The day before entering the hospital, that is, eight days after the injury, the man developed very painful clonic spasms in the muscles of the left side of the neck, which continued all night and during the next day, and the spasms could not be relieved by morphin. On entrance to the hospital the man could not swallow, the neck was rigid, the recti muscles were very tense and the jaws were somewhat rigid. The slightest stimulation caused severe painful clonic spasms in the left side of the neck and left shoulder. Fifteen hundred units of antitoxin were given subcutaneously and 20,000 units were given into a vein, and 16 cc of a 25 per cent solution of magnesium sulphate were ordered every five hours. The thumb was incised and serum was injected around the base. However, one dose of magnesium sulphate relieved the spasms, and the following morning the neck spasms were gone and the jaws and the recti muscles were relaxed. The man had slept well and was quite comfortable. The same evening another dose of magnesium sulphate was given, and 10,000 units of antitoxin were injected subcutaneously. The man was free from further spasms. On

November 21, nine days after admission, 3000 units of serum were given intramuscularly, and the patient was allowed to go home.

Comment. While rapid relief was present in this case, it undoubtedly was a case of local tetanus, progressing to general tetanus. A total of 34,500 units of antitetanic serum was administered.

CASE III.—F. C. W., a male, aged forty-one years, was referred to me at the Alexian Brothers' Hospital by Dr. J. J. Fitzgerald, December 16, 1922, with a history of having mashed his left index finger in an automobile spring three weeks before. The distal segment of this finger had been amputated, and the man had developed clonic spasms in his legs one week before admission. On entering the hospital, the patient had severe tonic spasms in his legs and recti muscles, with stiffness in the arms, and the least stimulation caused painful clonic spasms in the legs and abdomen, with opisthotonos. These symptoms had been getting worse for the previous six days, and the man could not lie in bed sufficiently quiet to permit a physical examination.

No trismus was present. Twenty thousand units of serum were given at once into a vein, and 16 cc of magnesium sulphate in 25 per cent solution were given subcutaneously every five hours. The wound in the finger which appeared to be healed was opened and considerable pus was found. It was kept open and cleaned out with tincture of iodin and hydrogen peroxide. On the following morning the symptoms were much improved. Some rigidity persisted, and short clonic spasms were caused by stimulation, but the man was fairly comfortable. Thirteen thousand units of serum were given into a vein. The next day, December 18, 20,000 units of serum were given intravenously and the magnesium sulphate was continued. Under this treatment, with average doses of morphin sulphate at times, the symptoms slowly improved day by day. The rigidity and clonic spasms continued to a lessened degree, but they were not considered severe enough to employ serum or magnesium sulphate, intraspinally. All medication was stopped, December 21, as the man presented symptoms of a bronchopneumonia and had a marked rash. The spasms increased somewhat, and magnesium sulphate was given again three times a day, beginning December 23, and again relieved the spasms. On December 24 10,000 units of serum were given into the muscles. Very short and slight clonic spasms of the recti muscles continued until December 26, when all spasms stopped. The man went home entirely relieved, January 13, 1923.

Comment. This was a very severe and exhausting case of well-developed tetanus. The effect of the magnesium sulphate was not so marked, but a gradual relief was effected. The improvement under subcutaneous injections of magnesium sulphate was satis-

factory, however, so that no other method of administration of the serum or magnesium sulphate was considered necessary. A total of 63,000 units of antitetanic serum was given in this case.

CASE IV.—V. K., a male, aged sixteen years, was seen in consultation with Dr. M. J. Glaser when the patient entered the Alexian Brothers' Hospital, February 7, 1923. The boy stated that his left index finger was lacerated by a piece of dirty, greasy metal from an automobile, about two weeks before entrance into the hospital. The wound had been sutured, but did not heal, and eleven days after the injury the boy noticed stiffness in his jaws and in his back. The following day he developed clonic spasms, which occurred on the slightest irritation.

On entrance to the hospital, which was three days after the onset of the symptoms, the patient presented marked opisthotonos, with retraction of the neck, board-like rigidity of the abdominal muscles, clonic and tonic spasms in the muscles of the jaws, spasm in the throat which prevented swallowing, stiffness in both legs and arms and greatly increased reflexes. The slightest stimulation would cause severe painful clonic spasms in the back, neck, jaws and abdomen. The symptoms had been progressing rapidly and the boy showed symptoms of great exhaustion.

Twenty thousand units of serum were given intravenously on entrance, and 5000 units were injected about the site of origin in the left index finger. The wound was opened, tincture of iodin was used freely and the wound was dressed so that air came in contact with it. Magnesium sulphate, 12 cc of a 25 per cent solution, were given subcutaneously every four hours.

The dose of magnesium sulphate was increased to 16 cc the evening of the same day, and 20,000 units of serum were given intravenously. The patient was resting easier and was able to swallow fluids freely during the evening.

On the second day, February 8, 10,000 units of serum were given intravenously, and the magnesium sulphate was continued in 16 cc doses every three hours. The spasms were less severe, and the boy was able to turn over in bed, but clonic spasms were frequent. However, a hypodermic injection of $\frac{1}{8}$ gr. of morphin sulphate permitted the boy to sleep.

On February 9 10,000 units of serum were given intravenously, and the magnesium sulphate was continued as before. On February 10 the boy's condition was much better; he could open his jaws wider, the abdominal spasms were less, the reflexes were less active and the boy was suffering no pain. The abdomen could be palpated without exciting spasms. Ten thousand units of serum were given intravenously. On February 11 and 12 the spasms were somewhat increased. The magnesium sulphate had been given at greater intervals. Ten thousand units of serum were given intra-

venously, February 11. The magnesium sulphate was again given at three-hour intervals, and on the evening of February 12 the spasms were lessened, but the boy was uncomfortable and exhausted. A subcutaneous injection of $\frac{1}{4}$ gr. of morphin sulphate permitted a restful sleep.

On February 13 the condition was much improved, the jaws were more relaxed, the abdominal muscles were soft and the legs were flaccid. Strong stimuli did not tend to cause spasms. From February 14 to 19 the condition improved. The clonic spasms became less in severity and frequency and disappeared. Some tonic spasms persisted, but the boy was comfortable. However, small doses of morphin produced restful sleep. Magnesium sulphate was given twice daily during this time. February 18 to 20 the clonic spasms increased, but they were controlled by increasing the magnesium sulphate. From February 21 to 24 the boy sat up in bed. Occasional jerks occurred in his arms and legs, but disappeared when the magnesium sulphate was given. On February 24 the boy was up in a chair. No spasms were present. He gained strength and gradually improved. On February 27 10,000 units of serum were given intramuscularly. The boy left the hospital, March 4, 1923, apparently entirely cured.

Comment. This was a very severe case of tetanus with considerable exhaustion. A total of 85,000 units of antitetanic serum was given. On several occasions the value of the magnesium sulphate was demonstrated when the spasms increased while the magnesium sulphate was discontinued, and further injections again controlled the spasms.

This case illustrates the marked effect of average doses of morphin when the patient is under the influence of magnesium sulphate. This point has been emphasized also by Gwathmey,[57] who states that combining the effect of magnesium sulphate with morphin sulphate, increases the value of the morphin from 50 to 100 per cent.

Painful exhausting spasms were relieved, and sleep occurred after $\frac{1}{8}$ to $\frac{1}{4}$ gr. doses of morphin on several occasions. Such doses of morphin in the absence of the relaxing effect of magnesium sulphate are powerless to control tetanic spasms. Furthermore, it seems that it is not necessary to push the effect of the magnesium sulphate to complete relaxation, and hence near the danger point. It is necessary only to control the spasms sufficiently to prevent exhaustion, at which point average doses of morphin may produce restful sleep.

Case Reports (by Dr. W. E. Leighton). CASE V.—H. B., male, aged twelve years, was seen in consultation with Dr. H. L. Nietert when the patient entered the Lutheran Hospital, July 10, 1922,

with a history of having shot himself in the index finger, July 3. He had been seen by a doctor, but no prophylactic antitetanic serum had been given.

On July 8 he began to complain of a stiff neck, and it was thought that he had a cold. On July 9 he was unable to open his mouth on awakening, and the jaw became fixed, but he had no convulsions. On admission to the hospital a small wad was removed from the finger with a curette. The cavity was sterilized with carbolic acid, irrigated with peroxide of hydrogen and packed with gauze, and a moist dressing was applied. Clonic contractions, involving the muscles of the jaw, neck and back were observed at this time. The temperature was 101° F.; pulse, 120; respiration, 36. During the day 20,000 units of antitetanic serum were given subcutaneously, and 10,000 units were given intravenously, with bromides and chloral hydrate.

The following day he was decidedly worse. He had a spasm, lasting ten minutes. He breathed heavily. During an attack he ground his teeth and frothed at the mouth. Opisthotonos was pronounced. During the day he had 25,000 units of antitetanic serum subcutaneously, intravenously and intraspinally, and subcutaneous injections of magnesium sulphate were begun. The temperature was 104° F., by axilla.

On July 12 spasms occurred every half hour during the night. The lips were blue and the breathing was shallow. During the day 40,000 units of antitetanic serum and 90 cc of magnesium sulphate were given subcutaneously. He was delirious at times. The following day the patient seemed better. Spasms occurred at longer intervals. He had one severe convulsion, lasting five minutes. Thirty thousand units of antitetanic serum and 90 cc of magnesium sulphate with chloral hydrate and $\frac{1}{8}$ gr. of morphin sulphate were given.

On July 14 he had one severe convulsion, lasting twenty minutes. The temperature was 102° F. As there was no improvement, it was decided to administer 2 cc of a 25 per cent solution of magnesium sulphate, intraspinally. Within two hours there was a decided improvement. There was marked relaxation of muscles and the patient felt better.

On July 15 and 16 he received 2 cc of the magnesium sulphate solution, intraspinally, and continued to show marked improvement. On July 17 he was so much better that it was decided to omit the intraspinal magnesium sulphate, but he was given 30,000 units of antitetanic serum and the subcutaneous injections of magnesium sulphate were kept up. During the night he had the most severe convulsion of all, and his condition was alarming. Magnesium sulphate, 2 cc, was given intraspinally, and within two hours relaxation had taken place. On July 18 relaxation was complete, and patient could turn on his side voluntarily. From this time on

the patient continued to improve, but 2 cc of a 25 per cent solution of magnesium sulphate were given intraspinally, and 5 cc subcutaneously, every four hours.

Muscular spasms, slight in character, kept up for several days, however, and did not entirely disappear until July 25. After this date the patient was up and about and was discharged, August 2, free from symptoms, except for an internal strabismus of the left eye.

Comment. This was an acute case of tetanus of five days' onset. The patient received in all 245,000 units of antitetanic serum and 815 cc of magnesium sulphate solution. He had 113 hypodermic injections without infection. In spite of the large doses of antitetanic serum, no improvement took place until the magnesium sulphate was given intraspinally, and after five intraspinal injections of 2-cc doses of magnesium sulphate the patient began to show improvement, and the convulsions were practically abolished.

I believe that without the use of magnesium sulphate, we would have lost this patient. The boy is perfectly well today, one year later.

The following 3 cases were from the services of Dr. Leighton and Dr. C. F. Sherwin at the St. Louis City Hospital.

CASE VI.—On July 13, 1922, a colored boy, aged fourteen years, was admitted to the City Hospital, complaining of stiffness in the neck and shoulders, with a history of having shot himself in the left index finger on July 4, 1922. The wound had been dressed, but no antitetanic serum had been given. Symptoms began on the eighth day. The left index finger was amputated. The muscles of the neck and abdomen were rigid, but there was no trismus. A well-marked convulsion occurred on the operating table. Thirty thousand units of antitetanic serum were given.

On July 14, the temperature was 106° F., and increased muscular rigidity and frequent convulsions were noted. On July 15, there was slight relaxation. Twenty thousand units of antitetanic serum were given. On July 16, attempts at opening the mouth caused convulsions. Nine thousand units of antitetanic serum were given. On July 17, 30,000 units of antitetanic serum were given. The abdomen seemed more relaxed. On July 18, 20,000 units of antitetanic serum were given. The patient was somewhat better. On July 19, 10,000 units of antitetanic serum were given. The patient did not feel so well, and refused to eat or drink. Trismus was marked. The head and neck bent backward, and the neck was rigid. On July 20, the patient refused to eat, as eating and drinking produced spasms. Marked rigidity of the neck and abdomen

was present. On July 21, 10,000 units of antitetanic serum were given. There was no improvement on July 22.

On July 23, 3 cc of 25 per cent solution of magnesium sulphate were given intraspinally, and relaxation of the muscles of the back and abdomen was noticeable within a short time. On July 24, the patient could move about with ease. The muscles were less rigid, and from this time the patient continued to improve until he was discharged. On August 2, he was up and about the ward, and appeared to be entirely cured.

Comment. This was a case of acute tetanus with an onset after eight days. Rigidity of the muscles continued in spite of 130,000 units of antitetanic serum. Relaxation appeared following 3 cc of magnesium sulphate intraspinally, and did not recur.

CASE VII.—A. W., aged forty-two years, entered the St. Louis City Hospital, August 25, 1922, with a history of having stepped on a nail, eighteen days previously. Five days before entrance he began to have a difficulty in mastication of food on account of the stiffness of the jaw. Three days later he was obliged to go to bed because of dyspnea. Stiffness of the muscles of the abdomen, neck and the arms was marked. On entrance the arms were flexed across the chest and were rigid. The neck was rigid and could not be flexed. Excursions of the chest were limited, and the abdomen was rigid. There was an anxious look on his face, and the jaws were locked. The legs were not rigid and motion was not restricted. A small scar, which was not tender, on the sole of the right foot, was excised under ether. The wound was cleansed with tincture of iodin, and a dry sterile dressing was applied. Sixty thousand units of antitetanic serum were given subcutaneously and intraspinally, and 6 cc of a 25 per cent solution of magnesium sulphate were administered subcutaneously.

The second day he received 20,000 units of antitetanic serum and 20 cc of magnesium sulphate subcutaneously in divided doses. There was no change in his condition. Spasms occurred at intervals of fifteen to twenty minutes. The third day there was some improvement. Spasms occurred only on external irritation, such as a sudden noise. He received 10,000 units of antitetanic serum and 20 cc of magnesium sulphate were given subcutaneously. On the fourth day the jaws became somewhat relaxed, and he was able to open them slightly. Ten thousand units of antitetanic serum and 20 cc of magnesium sulphate were given subcutaneously. On the following day he was much better, and the abdominal muscles were relaxed. From this time he steadily improved, and was able to move about in bed on the eighth day. No medication was given after the tenth day, and all muscular motions were normal on the fourteenth day.

Comment. The onset in this case took place on the thirteenth day. He received 90,000 units of antitetanic serum and 156 cc of a 25 per cent solution of magnesium sulphate, subcutaneously.

CASE VIII.—J. D., aged twelve years, entered the St. Louis City Hospital, September 11, 1922, with a history of having cut his foot on a rusty piece of tin, twelve days previously. Three days before admission he noticed that he could not open his mouth, and his jaws appeared stiff, and the following day he could not bend his neck. Muscular twitchings began on the day of entrance. On admission he had rigidity of neck, abdomen, back and legs. Opisthotonos was marked, and the respiration was labored. The jaws were locked. Under ether anesthesia the scar on the sole of the foot, which was partially healed, was excised. Fifty thousand units of antitetanic serum and 12 cc of a 25 per cent solution of magnesium sulphate were given subcutaneously. During the day convulsions were frequent, and were excited by the least external irritation.

On the second day he received 30,000 units of antitetanic serum and 12 cc of magnesium sulphate. During the day the patient said he felt better and could open the mouth slightly and he was less rigid. On the third day the patient could turn slowly in bed, he felt better and expressed a desire to eat. During the day 20,000 units of antitetanic serum and 18 cc of magnesium sulphate were given subcutaneously. The patient was very nervous. On the fourth day he received 12 cc of magnesium sulphate and 20,000 units of antitetanic serum. Slight opisthotonos persisted. During the next few days he improved rapidly, and was up and about the ward, with no abnormal symptoms present on the tenth day. He was able to open his mouth to the full extent on the seventh day.

Comment. The onset in this case was on the ninth day following the injury. He received 140,000 units of antitetanic serum and 78 cc of a 25 per cent solution of magnesium sulphate subcutaneously. On account of extreme nervousness he had an occasional hypodermic of morphin sulphate in average doses.

Discussion. We are convinced that the use of magnesium sulphate played a very important rôle in our success in these 8 consecutive cases of tetanus. They were all distinct cases of acute tetanus, and prophylactic serum had not been given in any case.

Magnesium sulphate should be used in proper amounts to produce results. The subcutaneous method should be tried first, but if results are not prompt, the intraspinal method should be employed. This condition was found in Cases V and VI, where prompt relief followed the intraspinal use of magnesium sulphate, after the subcutaneous method did not give satisfactory results.

As illustrated in Case IV, it is not necessary to produce complete relaxation by pushing the magnesium sulphate near the danger point. After the spasms have been relieved sufficiently to prevent exhaustion average doses of morphin often will complete the relief and permit restful sleep.

There can be no routine in the use of magnesium sulphate. The dosage and method can be determined only by close personal and frequent observation of the patient. Magnesium sulphate cannot cure tetanus in the last stages. It cannot restore completely exhausted tissues. Its effect purely is to prevent exhaustion and to keep the patient comfortable and alive and permit nourishment, until the toxin can be separated from the nerve cells and eliminated.

Use of antitetanic serum during the disease is necessary in order to counteract free toxin and to prevent further combination of the toxin with nerve cells. Thus, the effect of the neutralizing antitetanic serum and the sedative effect of the magnesium sulphate are necessary for the cure of tetanus.

Summary. The rational treatment of tetanus should be carried out as follows:

1. Prophylactic antitoxin, subcutaneously in all suspicious wounds, repeated again after ten days, especially if suppuration is present, or if an operation is to be performed.

2. Antitetanic serum should be given during an attack of tetanus. Intravenous administration may be satisfactory. Intraspinal serum should be employed in severe cases or where improvement is not satisfactory.

3. Spasms should be controlled by the subcutaneous injection of magnesium sulphate. In urgent symptoms or when the subcutaneous method fails intraspinal or even the intravenous route should be employed. Morphin sulphate, in addition to magnesium sulphate, may aid at times. Careful personal observation is necessary in order to judge the dosage and method of administration of magnesium sulphate.

4. The wound of infection should be opened and cleaned, and air should be allowed to reach it. Tincture of iodin should be used locally. Serum should be injected at the site of the wound to block the progress of the toxin.

5. An intramuscular or subcutaneous injection of serum should be given on the eighth or ninth day after the beginning of the treatment, in order to keep up the prophylaxis.

6. Fluids and nourishment should be supplied, and careful nursing is essential.

REFERENCES.

1. Nicolaier: Inaug. Diss. Göttingen, 1885.
2. Kitasato: Deutsch. med. Wchnschr., 1889, **15**, 635.
3. v. Behring and Kitasato: Deutsch. med. Wchnschr., 1890, **16**, 1113.

4. Donati: Arch. ital. di chir., 1919, **1**, 1.
5. Kuemmell: Berl. klin. Wchnschr., 1916, **53**, 414.
6. Tulloch: Proc. Roy. Soc., London (Series B), 1917–1919, **90**, 529.
7. Ashhurst: Arch. Surg., 1920, **1**, 407.
8. Speed: Med. and Surg., 1918, **2**, 499.
9. Stauff: Zentralbl. f. Chir., 1916, **43**, 916.
10. Bungart: Zentralbl. f. Chir., 1916, **43**, 917.
11. Vernoni: Gazz. d. osp. e d. clin., Milano, 1917, **28**, 955.
12. Montois: Ann. de l'inst. Pasteur, 1916, **30**, 330.
13. Courtois-Suffit, Giroux and Fernan-Widal: Prevention of Tetanus, Paris, Masson et Cie, 1916.
14. Gessner: Jour. Am. Med. Assn., 1918, **71**, 867.
15. Ochsner: Jour. Am. Med. Assn., 1918, **71**, 870.
16. Chavasse: Bull. et mém. Soc. de chir. de Paris, 1917, **43**, 1249.
17. Hutchings: Ann. Surg., 1919, **50**, 52.
18. Bérard and Lumière, Lyon chir., 1915, **12**, 404.
19. Du Bouchet: Bull. et mém. Soc. de chir. de Paris, 1917, **43**, 924.
20. Bergell and Levy: Therap. d. Gegenw., 1904, **45**, 396.
21. Murphy: Jour. Am. Med. Assn., 1904, **43**, 460.
22. Hercher: München. med. Wchnschr., 1915, **62**, 1126.
23. Meltzer: Am. Jour. Physiol., 1900, **3**, 9.
24. Meltzer and Auer: Am. Jour. Physiol., 1905, **14**, 366.
25. Meltzer: Med. Record, 1905, **68**, 965.
26. Meltzer and Auer: Am. Jour. Physiol., 1906, **16**, 233.
27. Meltzer and Auer: Jour. Exper. Med., 1906, **8**, 692.
28. Blake: Surg., Gynec. and Obst., 1906, **2**, 541.
29. Logan: Jour. Am. Med. Assn., 1906, **46**, 1502.
30. Miller: Am. Jour. Med. Sci., 1908, **136**, 781.
31. Hessert: Surg., Gynec. and Obst., 1909, **9**, 145.
32. Kocher: Corr.-Bl. f. schweiz. Aertze, 1912, **42**, 969; 1913, **43**, 97; 1915, **45**, 1249.
33. Robertson: Arch. Int. Med., 1916, **17**, 677.
34. Straub: München. med. Wchnschr., 1915, **62**, 341; ibid., 1915, **62**, 25.
35. Meltzer: Lancet, London, 1915, **1**, 1330.
36. Meltzer: Jour. Am. Med. Assn., 1916, **66**, 931.
37. Joseph and Meltzer: Jour. Pharm. and Exper. Therap., 1909, **1**, 369.
38. Meltzer and Lucas: Jour. Exper. Med., 1907, **9**, 298.
39. Peck: Proc. Soc. Exper. Biol. and Med., 1913–1914, **11**, 103.
40. Gates: Proc. Soc. Exper. Biol. and Med., 1913–1914, **11**, 102.
41. Pribram: Jour. Am. Med. Assn., 1918, **71**, 869.
42. Park and Nicoll: Jour. Am. Med. Assn., 1914, **63**, 235.
43. Nicoll: Jour. Am. Med. Assn., 1915, **64**, 1982.
44. Bruce: Lancet, London, 1917, **1**, 680.
45. Andrews: Lancet, London, 1917, **1**, 682.
46. Golla: Lancet, London, 1917, **1**, 686.
47. Stone: Jour. Am. Med. Assn., 1922, **78**, 1939.
48. Kreuter: Beitr. z. klin. d. Infek., 1916–17, **5**, 189.
49. Vaillard: Jour. State Med., London, 1914, **22**, 513.
50. Speed: Surg., Gynec. and Obst., 1916, **22**, 443.
51. MacConkey and Zilva: Brit. Med. Jour., 1916, **1**, 411.
52. Teale and Embleton: Jour. Path. and Bacteriol., 1919, **23**, 50.
53. Kuemmell: Beitr. z. klin. Chir., 1915, **96**, 421.
54. Tullidge: New York Med. Jour., 1916, **103**, 1022.
55. Bruce: Brit. Med. Jour., 1917, **1**, 118.
56. Weston and Howard: Am. Jour. Med. Sci., 1923, **165**, 431.
57. Gwathmey: Jour. Am. Med. Assn., 1921, **76**, 222.
58. Buzello: Ztschr. f. ärztl. Fortbild., 1922, **19**, 427.
59. Ritter: Berl. klin. Wchnschr., 1915, **52**, 126.

OBSERVATION OF FAT DIGESTION FOR CLINICAL STUDY AND PHYSIOLOGICAL DEMONSTRATION.

By Anthony Bassler, M.D., F.A.C.P.,
and
J. Raymond Lutz, B.S., M.D.,
new york.

A procedure is herewith advanced in which the digestion of fat as it takes place in the human body may easily be observed, one in which the admixture of fat with pancreatic juice and bile occurs *in vivo*, one of some value in clinical study, and of value in a physiological department.

These observations were made during a period of the work of studying pancreatic function which consummated in the test for pancreatic function which one of us has devised. The findings were made during the work of studying lipolytic action and were so interesting that they seem worthy of separate presentation.

Procedure. In the morning, having taken no breakfast, the individual swallows the duodenal tube with the assistance of water. When the tip is well out in the duodenum (proven by fluoroscope) a few moments are allowed to elapse to permit the last of the water to leave the stomach. The patient then drinks about 60 cc of olive oil and lies on the right side. Gentle aspiration by means of a suction bulb and an intervening bottle of about 250 cc capacity is employed, which is kept in a water bath of 104° F. In an average time of nine minutes a characteristic return from the duodenum appears. As soon as the oil returns and at frequent intervals a drop is placed on a slide without cover glass and observed for fifteen to thirty minutes. A warm stage is preferred but the phenomena to be described also occur in the cold. The high dry objective is used in order to get best details.

Emulsification. This consists of oil with duodenal juice and bile. The oil will be found to have been more or less emulsified—the first stage of fat digestion. Usually the first return of the emulsion is coarse but may be fine, even finer and more uniform than the fat globules in milk which is looked upon as a perfect emulsion. In all periods of the aspiration the return contains the emulsion which gets finer. Investigation suggests that the emulsification of fats in the body takes place, not by agitation as occurs commercially when making an emulsion, but chemically. The bile, or certain constituents of it, acting on the oil, produces the emulsion. At various times an occasional globule has been seen very actively to break up into smaller globules by rolling along with pseudopods trailing after it which break off into a number of much smaller globules. When formed, the emulsion remains so for some time;

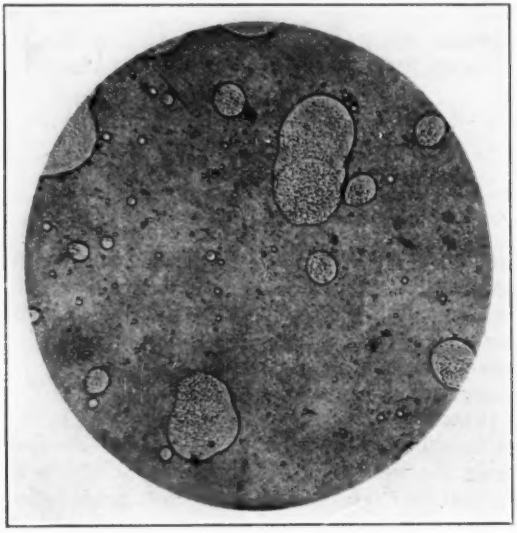


FIG. 1.—Showing stippling.

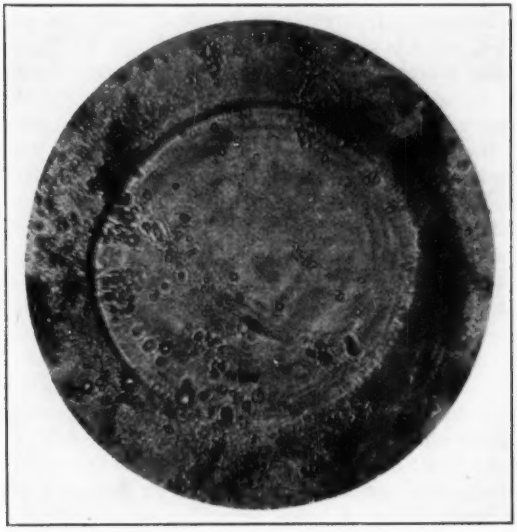


FIG. 2.—Showing rivulation.

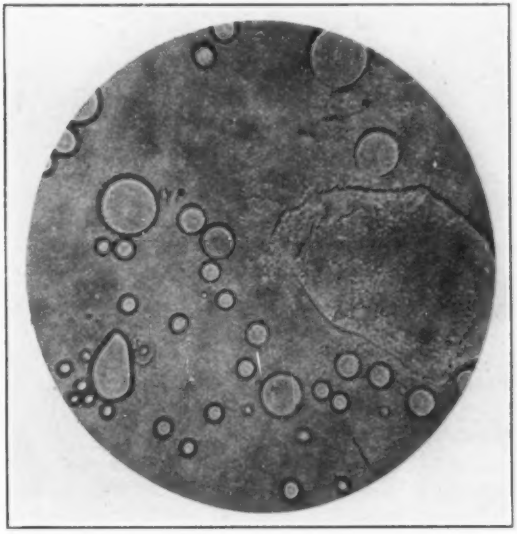


FIG. 3.—Showing rapid dissolution of the surface of the globule.

FIG. 4.—Showing corona of soap and pseudopod.

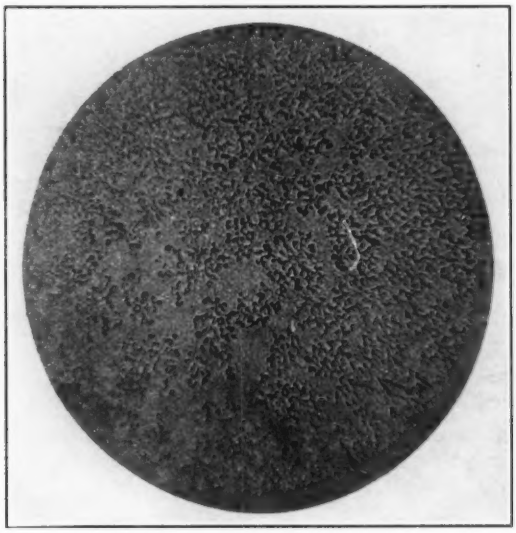


FIG. 5.—Complete soap formation.

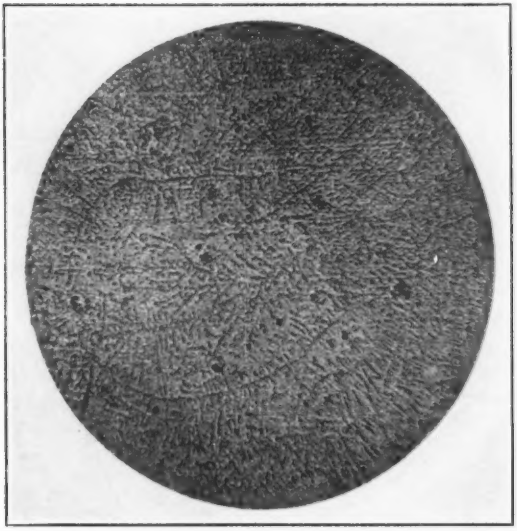


FIG. 6.—End-stage of fatty acid formation (palmitic acid crystals).

these provisions make it possible for lipolytic action on the fat to continue in the easiest and most vigorous ways. This emulsification continues in the duodenum whether the contents are acid or alkaline and will continue outside until an intense acidity occurs from fatty acids. As the emulsion becomes more acid the globules coalesce and the oil forms a layer on the top of the mixture. Watching the globules coalesce through the microscope shows the whole field in active commotion. At certain periods this is so lively that the whole field will change every few seconds.

SAPONIFICATION. The phenomena here may be described as what may be observed within and without the fat globule. Usually these are found going on together or one globule in the field may show one phase and another the other.

Watching the individual globules, even those of considerable size, shows as the first change one of two phases. The first may be designated as striation, and consists of a series of wrinkles or striæ, running more or less parallel across the globule, the process being gradual and progressive. These are very active when present but may not be observed in some returns. It probably is produced by some tension effect plus the action of lipase on the surface of the globule. These striæ are gradually increase in number and size and appear like wrinkles on a shriveled apple. The striæ are visible in the process of formation for fifteen seconds to two minutes when the globule turns over, the striæ or wrinkles disappear and a clear homogeneous globule of oil is again seen. This process of striation and returning to the original form may take place over and over for an indefinite number of times but after one to fifteen minutes they go on to the next stage, that of stippling. This may follow striation but can occur as an initial performance. One notices here a few granule-like bodies forming on the surface of the globule and in a short time the entire globule becomes that way. The whole interior of the globule may be in active motion, the globule itself being at rest. When the stippling or granulation has reached a certain stage of density or concentration they slide off to the periphery of the globule and into the surrounding medium. The process of stippling and casting off of particles of material repeats many times until the globule is about one-half the original size or smaller. Waves of refractive material occasionally are seen running concentrically toward the periphery of the globule and into the surrounding liquid and appear like waves of melting butter running off from a ball of butter being heated from above. These waves of material as they leave the globule disappear and are dissolved in the surrounding medium. This material, we believe, is soluble soap. This phenomena we have designated "rivulation." During the stippling process, bud-like projections of soaplike amebic pseudopods may form, become solidified, and either break off from the remainder of the globule or remain attached to it. More buds form at various

points around the periphery (spherical) and go through the same process. Due to budding, rivulation and the slipping off of the stipplied surface to the periphery, there soon accumulates a corona of solid, irregular immobile material which we believe to be soap. The field then contains free masses of this soap as some of it slips away from the parent globule. Rarely granular material may be seen to form within the globule and suddenly burst through the wall of the globule with considerable force. The corona of soap is very frequently many times the size of the original globule which has become smaller. After the formation of the corona the process stops, probably because of concentration of (fatty) acids. If the slide is allowed to stand for some time (to dry) most of the field will be found to be composed either of masses of soap or covered with the feather-like palmitic acid crystals. A clear, colorless, oily fluid remains which does not dry and is probably glycerine. Not infrequently globules will be seen to coalesce suddenly with a colorless irregular shaped oily material seemingly laking or being dissolved into it and losing its original yellow, oily consistency. This is a sudden complete conversion of the globule into soluble soap which is dissolved. Not infrequently the globules will from fully filled fat globes break up by the globules disappearing, leaving large masses of soap and fatty acid crystals and a certain portion of colorless liquid (glycerine).

Perhaps the most interesting of all of the phenomena are the soap projections that occasionally occur from a complete fat globule. These occur in one of two ways. The first is the sudden protrusion of a portion of the capsule that closely resembles the pseudopodium of an ameba, but differs from it in that the globule remains quiet. Two or more of these may occur from the sides of the same globule. Apparently they are portions of soap that have been excluded from the neutral fat of the globule. The second form is the extrusion of the soap from the globule in small particles, these generally adhering to the sides of the fat globule, their number accumulating.

FATTY ACID FORMATION. This is observed as a part or accompaniment of the phases described above. Here and there the crystals are met with, and if a slide is allowed to stand for an hour or two they will be observed intermingled with small deposits of soap and usually a large drop of glycerine on one part of the slide.

Summary. The phenomena described can be used as a clinical test for lipase activity. It is, of course, not quantitative in any definite sense but when one has made these observations a number of times a judgment of value is soon acquired.

For physiological demonstration in medical schools and elsewhere there is no easier, striking and quickly performed demonstration of lipolytic action of the pancreas than this. Enough material can be obtained from one individual tested to supply sufficient material under the microscope for a large number of students.

PRIMARY CANCER OF THE LIVER*

By Julius Friedenwald, M.D.,

and

Hiram Fried, M.D.

(From the Gastro-Enterological Clinic of the Department of Medicine of the University of Maryland.)

The variety of primary carcinoma of the liver renders this affection of sufficient interest to warrant the report of even a single case. It is generally admitted that data concerning the incidence of this disease to 1870 are unreliable; inasmuch as up to this period the metastatic types were not definitely differentiated from the primary forms. In Hansemann's[1] 258 cases of carcinoma of the liver, four (1.5 per cent) were primary. Eggel[2] noted 163 cases of primary carcinoma of the liver up to 1901 and Goldzieher and von Bokay[3] observed 18 cases in 6000 autopsies (0.3 per cent). In 1911 Karsner[4] reported 9 cases and in 1913 Winternitz[5] 3 cases occurring in 3700 autopsies at the Johns Hopkins Hospital (0.08 per cent) while in 1923 Clawson and Cabot[6] report a single case in 5100 autopsies at the University of Minnesota. Lichty and Richey,[7] in 1922, report 3 cases observed by themselves and note that the incidence of this disease varies in different clinics from 0.13 to 1.3 per cent with an average of 0.5 per cent in the collected autopsy reports. Torland[8] reported 10 cases in 10,000 autopsies performed for all causes.

Report of Case. A. N., single, female, aged fifty-two years, consulted us April 28, 1921. She complained of abdominal discomfort especially located in the upper right abdomen, which had been annoying her for several years, but which had gradually become more aggravated during the past year. In addition there has been pressure and distention in the lower abdomen at times with occasional nausea, acidity of the stomach, eructations, bitter taste in the mouth, and constipation. The patient has not had any previous serious illnesses and her family history was unimportant. She had lost 10 pounds in weight.

On physical examination, there was evidence of loss of flesh, and the scleræ and skin present a slight icterus. Her weight was 106 pounds; the pulse, temperature and respirations were normal. The blood-pressure was 140/80. The heart and lungs presented no abnormalities. The abdomen was soft, extremely relaxed; the liver extended slightly below the costal arch and there was a slight degree of tenderness in this area as well as in the lower abdomen. The spleen was not palpable. The urine was normal, with the

* Presented at the Meeting of the Association of American Physicians, Atlantic City, N. J., May 7, 1924.

exception of a trace of bile, which it contained on a number of examinations. The tests for albumin, sugar and casts were always negative. The Wassermann blood test was negative. The hemoglobin was 80 per cent; red blood cells numbered 4,200,000; leukocytes, 6400. The gastric contents, following an Ewald test breakfast, revealed a total acidity of 53; free HCl, 42. The stool was of medium size, semisolid and fairly light in color and contained a slight quantity of mucous and undigested food matter; blood was not present.

The non-surgical biliary drainages presented turbid bile, somewhat greenish in color, but containing large fractions of "B" bile, with cholesterin crystals and mucus, and revealed in addition a definite colon infection.

The roentgen-ray report was as follows: Prolapsed fish-hook stomach, actively contracting and pulled over and held in the upper right quadrant; no defects; duodenal cap not deformed; colon prolapsed and spastic; cæcal stasis.

The diagnosis arrived at was cholecystitis with possible beginning cirrhosis of the liver.

Under a six weeks' rest cure in addition to frequent non-surgical biliary drainages, the patient improved markedly in health with relief from all abdominal distress. All evidence of the slight jaundice heretofore noted had disappeared; she made a gain of 10 pounds in weight, and with the exception of occasional headaches, appeared to enjoy normal health.

On April 22, 1922, a year following her first visit, she again returned with a history of having a drawing discomfort in the upper right quadrant of the abdomen with distention during the preceding two weeks, together with a progressively increasing jaundice. On examination, the liver was found apparently smaller than at the previous examination, and a large quantity of free fluid was noted in the abdomen. The skin and scleræ were deeply jaundiced.

Operation was advised and performed on the following day. About 500 cc of a straw colored fluid escaped from the abdominal cavity; the liver was found small, hard and definitely cirrhotic and contained numerous nodules. An omentopexy was performed. The patient quickly recovered from the affects of the anesthetic and apparently was doing well for the first twenty-four hours. She then lapsed into a deep coma, developed fever (101° to 102°) and died on the third day following operation.

Autopsy (No. 71). Performed one hour and forty minutes after death.

Anatomical Diagnosis. Primary carcinoma of the liver, cirrhosis of liver, hemorrhagic ascites, jaundice, right sided pleurisy with effusion, pulmonary edema, acute bronchopneumonia, chronic nephropathy, chronic pericarditis, hour-glass stomach, cervical polyp, anemia, emaciation and edema of the extremities.

Protocol. The body is that of a white woman, 163 cm. in length; rigor mortis has set in. There has been evident loss of weight as is shown by the looseness of the skin and the loss of subcutaneous fat. The scleræ are very yellow. Nose and mouth are negative. Both jugulars are distended and stand out prominently. There is a network of dilated veins over both shoulders. None are seen on the abdomen. There are 2 abdominal incisions; (1) An upper right rectus, through which two cigarette drains and a rubber tube projects; (2) a low midline incision starting at the umbilicus and extending 10 cm. toward the pubis.

The *lungs* show a marked congestion and edema with fresh pleural adhesions and areas of bronchopneumonia. The mediastinal glands are as large as army beans and black. There are no gross areas of new growth.

The *abdominal cavity* contains a large amount of blood-tinged yellow fluid. The omentum is sutured outside the abdominal cavity in the midline incision to the sheath of the rectus muscle. It is red and granular in this portion but not strangulated. The jejunum looks edematous and its walls are thick and rubbery, as if hypertrophied. This condition extends to the ileum which seems normal. The appendix is long, thickened and attached to a band of adhesions, which extends from the lateral abdominal wall to the cecum. The stomach has a constriction in its middle portion, and is edematous like the jejunum. The duodenum is greatly dilated; C-shaped and also very edematous.

The *liver* is smaller than normal; measures 22 by 14 by 7 cm. and weighs 1000 gm. The surface is coarsely granular with nodules studded over the surface varying in size from a few millimeters to several centimeters. The left lobe is almost separated from the rest of the liver by a deep fissure, and consists almost entirely of one large nodule, measuring 8 by 2 cm. The nodules vary in color from a very deep brown to a light opaque yellow, which resembles fat. In certain areas, the tumor invades the lumen of the portal veins and bile ducts. Where liver parenchyma still remains, it is of a deep greenish-brown or a grass-green color. Gray translucent bands of fibrous tissue can be seen both surrounding the nodules and permeating between lobules of liver parenchyma.

It is interesting to note that extrahepatic nodules were conspicuous by their absence. The lymph nodes showed evidence of chronic inflammation, but no new growth was made out either in the gross or microscopical examination.

Microscopical Examination of Liver. The portions of liver parenchyma not involved by new growth are the seat of a marked cirrhotic process. This is irregularly distributed and involves mainly the periportal spaces. Where new growth is present, the cirrhosis is still more marked. Here and there in the cirrhotic areas are clumps of round cells. The tumor assumes a trabecular arrangement,

sometimes presenting as long strands of single cells resembling normal liver parenchyma; elsewhere, as columns of three or four cells abreast. As has been frequently observed, the tumor cells are easily differentiated from normal liver: (1) By their smaller size; (2) by their increased affinity for hematoxylin; (3) by their lack of pigment (hemosiderin); (4) by the occasional presence of mitotic figures.

Discussion. Primary carcinoma of the liver may occur at any period of life; more frequently in males between the fortieth and sixtieth years. Griffith[9] collected 57 cases in children from the first to the sixteenth years of life; Danzie[10] 23 cases under two and a quarter years and Rolleston[11] 32 under ten years. The following table taken from Yamagiwa[12] indicates the occurrence of this disease as to sex and age.

	Liver-cell cancer.		Bile-duct cancer.	
Age.	Eggel.	Yamagiwa.	Eggel.	Yamagiwa.
1 to 10 years	1	2	1	0
11 to 20 years	2	1	0	0
21 to 30 years	7	2	2	0
31 to 40 years	12	5	2	0
41 to 50 years	13	2	2	3
51 to 60 years	28	9	1	4
61 to 70 years	22	0	4	1
Over 70 years	8	0	1	0
Not indicated	0	6	0	7

	Liver-cell cancer.		Bile-duct cancer.	
	Male.	Female.	Male.	Female.
Yamagiwa	17 (80.95%)	4 (9.5%)	4 (50.0%)	4 (50.0%)
Eggel	65 (68.40%)	30 (31.6%)	6 (42.9%)	8 (57.1%)

According to Winternitz the malignant epithelial tumors of the liver may be divided into those arising from the bile ducts and those from the liver cells. The appearance of the bile pigment in distinguishing these types is only of relative importance inasmuch as while the bile stained nodules are ordinarily derived from the liver cells, tumors developing from small bile ducts may also have bile pigment contained within their lumina. They may be distinguished however, from a microscopical point of view, *i. e.* by their tendency to conform to the structure of the tissue from which they develop, the bile-duct cancers occurring as tubulo-adenomatous and the liver-cell cancers as trabecular structures.

The relation existing between primary carcinoma of the liver and cirrhosis has been a matter of considerable interest.

According to Winternitz's tables and analysis, a large proportion of cases of primary cancer of the liver are associated with cirrhosis and cirrhosis is definitely more frequently observed in cancers arising from the liver cells than in those from bile ducts. Karsner[4] also agrees that cirrhosis is observed to some degree in almost all cases of primary liver cancer, and Pirie[13] calls attention to the occur-

rence of cirrhosis as an associated factor in many instances of this disease in the natives of Africa infected with schistosomiasis, inasmuch as this form of infection has been proven to be a frequent cause of cirrhosis.

While the largest proportion of cases of cancer of the liver are associated with the annular type of cirrhosis, other forms as syphilitic or those due to echinococcus cyst infection occur.

A number of theories regarding the relation of cirrhosis to the new growth have been advanced. Certain observers maintain, that the two conditions occur entirely independently of each other, others that the cirrhosis is a causative factor or that the two diseases are a result of the same etiological factor and still others, that the cirrhosis is secondary to the tumor.

According to Winternitz the relation of cirrhosis to carcinoma can be best explained on the following bases. Due to injury, a destruction of liver tissue occurs on account of which fibrosis and regeneration takes place. This is followed by a production of hyperplastic nodules of liver cells and bile-duct structures, ordinarily observed in cirrhosis. These formations have the appearance of true adenomata. On account of the continuance of the injury the necrosis and regeneration continues, the cells lose their function and through an excessive proliferation develop into malignant growths. According to this investigator therefore, the nodular hyperplasias, often indistinguishable from true adenomata are the source of the carcinomatous growths, and therefore all cancers must develop through the benign or adenomatous stage.

While the multicentric development of the primary cancer of the liver has been maintained by many investigators (v. Heukelom,[14] Travis,[15] Goldzieher and Bokay,[3] Yamagiwa[12]); others (Ribbert,[16] Karsner[4] and Winternitz[5]) hold that these growths are unicentric in origin.

Metastases are not very frequent, occurring mainly in the thoracic and mesenteric lymph glands, omentum, lungs and other parts of the liver. According to Eggel,[2] of 163 cases collected 40 presented no secondary involvement, 50 showed growths only in the portal and hepatic branches, 30 had metastases in the lungs and thorax, 18 in the lymph nodes and 9 involved the colon, pancreas, ovary, kidneys, omentum, thyroid and cranium, respectively. Catsaras[17] was unable to ascertain but a single instance in which metastases were noted in several bones from primary cancer of the liver. He described a case with metastases in the head and neck of the femur. Ewing[18] notes that extrahepatic metastasis occurs much earlier and is more frequent in biliary than in hepatic carcinoma. It is an interesting fact that in many instances of extrahepatic metastases in primary carcinoma of the liver, bile has been observed in these growths.

According to Ewing[18] primary carcinoma of the liver may be

divided into 3 distinct groups: (1) The primary massive liver cells carcinoma; (2) the multiple liver cell carcinoma; (3) the carcinomatous cirrhotic forms.

The first variety occurs aside from the cirrhosis which may accompany this growth and but few symptoms are noted until near the termination of the disease. This growth represents a rapidly developing malignant form of solitary adenoma. It is met with as a large single yellowish friable mass in either the entire right or left lobes; metastases in various portions of the liver are not uncommon. The consistence of the mass is soft and as the result of an extensive liquefaction necrosis and hemorrhage a cystic formation may be produced with rupture into the peritoneum. The histological structure presents wide variation, but retains, at certain areas at least, its resemblance to liver cells. Ewing describes four distinct histological variations in structure: (*a*) Trabecular adenocarcinoma containing large granular acidophile cells as well as giant cells; (*b*) alveolar adenoma with areas consisting of groups of smaller granular epithelium surrounded by wide capillaries; (*c*) peritheliomatous areas containing capillaries surrounded by cubical granular cells, (*d*) diffuse carcinoma. In many of the necrosed areas the normal arrangement of cells disappears, and the growth consists of diffuse round or spindle cells with hyperchromatic nuclei.

In the second group—the multiple liver cell carcinoma—is classified the very malignant rapidly progressive forms in which cirrhosis is absent or is very slight. Ewing claims that no sharp division can be made however between this form, the solitary massive carcinoma, and carcinomatous cirrhosis forms. In this variety the liver is enlarged and presents many nodules which are grayish or bile stained, hemorrhagic or necrotic. Many of the smaller nodules are probably secondary. Metastases are infrequent but extensions to the diaphragm and gall-bladder are not unusual. Histologically, this form of carcinoma presents a number of variations, according to the area examined; these may be according to Ewing, trabecular carcinoma with giant cells, small alveolar carcinoma with many capillaries and diffuse carcinoma. Encapsulation of tumor masses is not noted. Clinically, this affection is extremely rapid in its course, in many instances terminating within a few weeks to a few months and at times the patient may succumb suddenly without having had any previous indication of a serious illness. Jaundice is not ordinarily observed but serous or bloody peritoneal effusions are not unusual. This affection is usually characterized by rapid emaciation and cachexia with enlargement of the liver and ascites.

The third group represents the carcinomatous cirrhosis forms. In this variety there is rapid increase in hyperplasia, invasion of veins and at times metastases. The growth is closely related to the cirrhosis and consequently the clinical signs are, in a measure, those

observed in this disease. The liver is ordinarily of the contracted type, but may be of normal size or greatly increased presenting multiple nodules often bile stained. The nodules may be extensive, numerous and usually involve the entire liver. In addition a definite portal cirrhosis is noted, and the nodules themselves are involved in connective tissue. It is not uncommon for the liver to present the typical appearance of hypertrophic cirrhosis. Microscopically, the liver presents an extensive replacement of parenchyma by adenomatous and carcinomatous nodules.

There is hyperplasia and hypertrophy of cell groups in the lobules. The cell groups enlarge into nodules, and produce atrophy by pressure on the remaining tissues. The cells of the growth are large producing thickened liver bands or the nuclei by increasing rapidly produce numerous smaller cells. Nuclear division of the amitotic type, giant-cell and syncytial masses, and fatty degeneration are conditions frequently observed. Cancerous cirrhosis, while usually noted in individuals over the fortieth year of life, is also found in young persons, previously in good health, gradually developing the symptoms of cirrhosis, *i. e.* jaundice and ascites. In fact the usual symptoms of cirrhosis precede the onset of carcinoma, which is finally revealed by the cachexia, progressive anemia, indigestion, hemorrhages, with a fatal termination within a few weeks or months. Clinically, there are but few distinctive signs of this affection; though at times the disease develops as a tumor formation with the growth in the region of the liver, and with the usual history of carcinoma in individuals previously in good health. In others the disease may be latent and may only be detected at autopsy in individuals succumbing to cirrhosis or other affections. In another class of cases the carcinoma is preceded by the usual signs of cirrhosis and finally terminates with the development of a rapidly growing tumor in the hepatic region. In all instances the presence of a carcinoma must be suspected by the rapid emaciation, secondary anemia and cachexia. Fever is not unusual in those instances with rapidly growing masses, especially in the terminal stages of the disease. Gastro-intestinal disturbances are common, and not infrequently dull dragging discomfort and pain in the right side and back. According to Torland[8] icterus is present in 63 per cent of cases; ascites in 58 per cent; general edema in 41 per cent; splenic tumor in 32 per cent; fever in 14 per cent. Eighty-six per cent of the cases are associated to a more or less degree with cirrhosis.

The prognosis is extremely grave, and Hale White[19] maintains that a fatal outcome usually occurs within four months following the first appearance of signs of malignancy of the liver.

REFERENCES.

1. Hansemann: Berl. Klin. Wchnschr., 1890, **27**, 353.
2. Eggel: Beitr. z. path. Anat. u. z. allg. Path., 1901, **30**, 506.
3. Goldzieher and v. Bokay: Virchows Archiv, 1911, **203**, 75.

4. Karsner: Arch. Int. Med., 1911, **8**, 238.
5. Winternitz, Johns Hopkins Hosp. Rep., 1913, new series, No. 3.
6. Clawson and Cabot: Jour. Am. Med. Assn., 1923, **80**, 13, 909.
7. Lichty and Richey: Ann. Clin. Med., 1922, **1**, 165.
8. Torland: Northwest Med., 1922, **21**, 253.
9. Griffith: Am. Jour. Med. Sci., 1918, **155**, 79.
10. Danzie: Lancet, 1922, **2**, 228.
11. Rolleston: Diseases of the Liver, Gall-Bladder and Bile Ducts, 1905, p. 469.
12. Yamagiwa: Virchows Archiv., 1911, **208**, 437.
13. Pirie: Med. Jour. South Africa, 1921, **17**, 87.
14. v. Heukelom: Beitr. z. path. Anat. u. z. allg. Path, 1894, **16**, 341.
15. Travis: Johns Hopkins Hosp. Bull., 1902, **12**, 108.
16. Ribbert: Das Karzinom, Bonn., 1911; Deutsch. med. Wchnschr, 1909, **35**, 1607.
17. Catsaras: Ann. de méd., 1921, **10**, 295.
18. Ewing: Neoplastic Diseases, W. B. Saunders, 1919, 2d ed., p. 682.
19. Hale White: System of Medicine (Allbutt and Rolleston), 1908, **4**, 1, 215.

THE PATHWAYS OF THE MEDIASTINUM, THE LUNGS, AND THE PLEURÆ.*

By J. Curtis Lyter, M.D.

Assistant Professor of Internal Medicine, St. Louis University School of Medicine; Visiting Physician to St. Anthony's Hospital and to the St. Louis City Hospital, St. Louis, Mo.

To anyone with the opportunity to observe closely the inception, progress, and termination of active pulmonary tuberculosis, there comes a time when an experimental explanation of some of the observed phenomena is desperately sought. This has probably become more certain with the development of the technic and study of pulmonary stereoroentgenograms. While pulmonary stereoroentgenography has aided very materially in the clinical study of pulmonary diseases, it has, by its own merits, forced the clinician into some newer fields of thought.

One phase of chronic, progressive, pulmonary tuberculosis which has been especially attractive to clinical thought is the apparent migration of the tubercle bacilli from the primary lesion to other portions of the same or the opposite lung. This apparent migration is probably best observed, in a clinical way, by a study of serial stereoroentgenograms taken at regular intervals in those cases revealing a steady progress of the pulmonary pathology. During the clinical and laboratory study of these cases the sputum should be proved to be bacilli free, thereby excluding the possibility of aspirated secondary lesions confusing the situation. Under serial stereoroentgenographic observation, as well as by frequent physical examinations, one is frequently able to observe the development of lesions at various sites of the same or opposite lung, follow the prog-

* From the Department of Internal Medicine of the St. Louis University School of Medicine and St. Anthony's Hospital.

ress of the primary lesion noted at the initial examination to be in one apex only. The clinical and stereoroentgenographic observation of the development of multiple lesions throughout the one or other lung would appear convincing as to the migration of the organisms from the primary lesion to various portions of either lung.

A second solution which does not consider the migration of the organisms necessary is that in which multiplicity of the sites of the primary infection is taken as an explanation of the multiple lesions observed during the course of all fatal cases. To accept this solution one must believe that during the initial invasion of the organisms they were implanted at various sites in each lung and that from the primary implantation the multiple pathological lesions developed during the progress of the disease.

Regardless of the conception one may entertain regarding the pathway traversed by the organisms in gaining access to the lung, it probably remains true that there exists only one site of primary infection and that the lesions which successively develop throughout one or both lungs during the progress of the disease have their origin in the one primary lesion by reason of the migration of the bacilli from the primary lesion to various sites in the same or across the mediastinum into the opposite lung.

From the clinical point of view, the migration of the organisms seems certain but when the phenomena are viewed from the anatomical aspect the migration of the organisms seems altogether impossible. From this aspect the migration seems impossible because of the very structure of the pulmonary lymphatics which heretofore were considered the only pathways open to the migrating organisms. The work of Miller seems to prove conclusively the presence of valves in the lymph trunks passing through the septa of the secondary lobules. Near the lung periphery these valves point toward the pleura and would seem to be a direct injunction against the passage of any material from the pleural surface through the lymphatics into the lung substance. A second set of valves were described by Miller as being located in the lymph trunks near the hilum. These valves point toward the hilum and have been presumed to prevent the passage of any material from the hilum into the lung substance. From the presence of these two sets of valves the lung substance seems protected against the entrance of any material by way of the lymph trunks. If these valves do exist and have the function seemingly indicated by their anatomical structure and position, they should act as an impediment to bacteria or other material passing into the lung substance from the pleural surfaces, subpleural spaces, or mediastinum merely because they would seem to indicate a flow of lymph only from the lung substance toward the pleura or toward the hilum.

The results of Miller's work have been disputed by some very

able anatomists but his own plates are so very convincing as to lead one to the conclusion that such valves do exist.

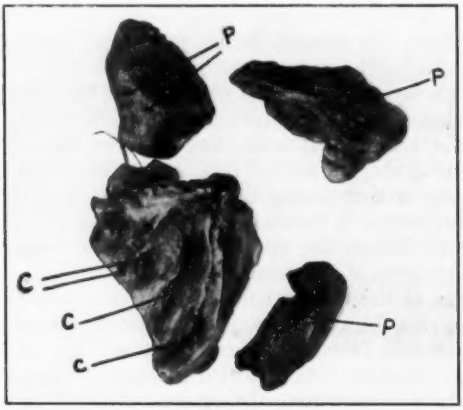


FIG. 1.—Showing masses of pigment beneath the visceral pleura indicated by *P*, and beneath the parietal *C*.

Experimental. Be the anatomy as it may, there are some phases concerning the clinical aspect of multiple lesions which, to the

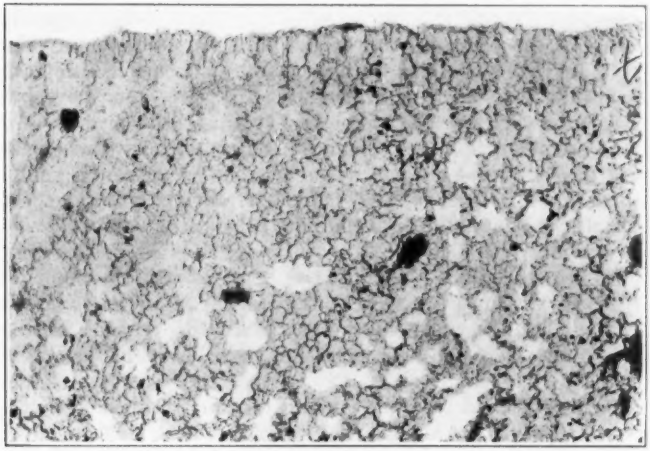


FIG. 2.—The left lung of a sheep whose mediastinum has been injected with India ink. Showing numerous accumulations of the pigment.

clinician, seem to demand an experimental investigation. This investigation was undertaken in the laboratories of St. Anthony's

Hospital to determine the probability of material passing from the mediastinum into the substance of the lungs and the probability of the same kind of material passing from the pleural surface into

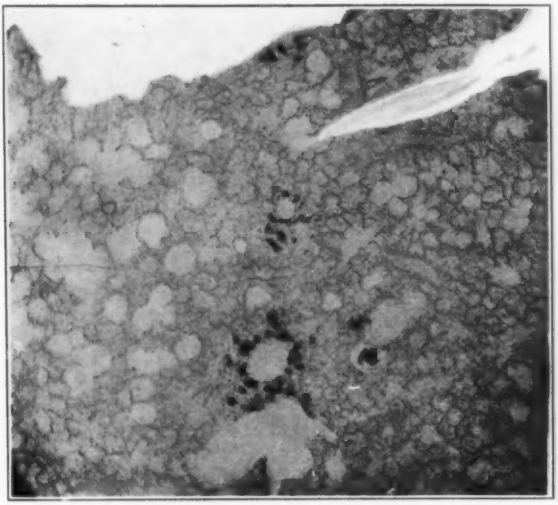


FIG. 3.—Right lung of the sheep described in Fig. 2.

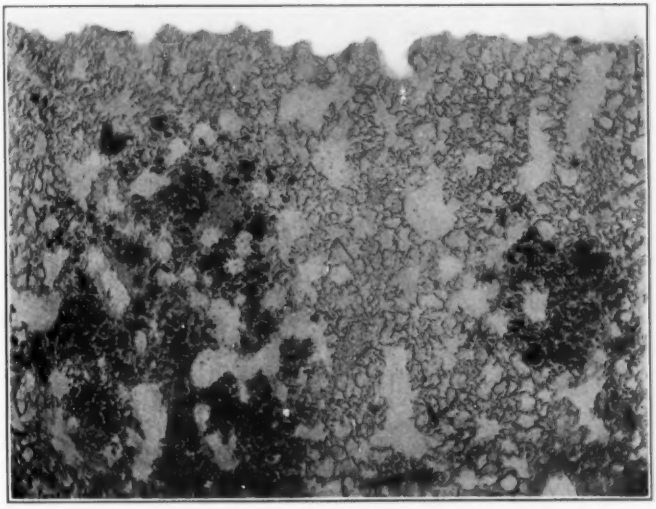


FIG. 4.—Right lung of a sheep where the right pleural cavity had been injected with India ink.

the lung substance. We were not primarily concerned about the pathways or means taken by the materials in passing into the lung substance, but were only concerned with the question of the existence of such a passage. For purposes of the investigation guinea-

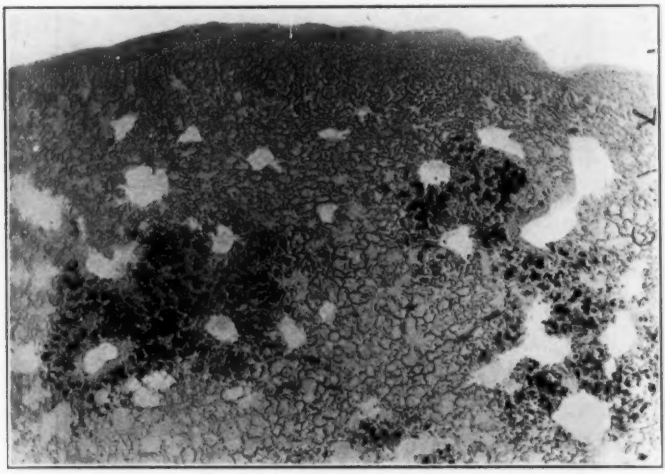


FIG. 5.—Left lung of a sheep where the right pleural cavity was injected with India ink.

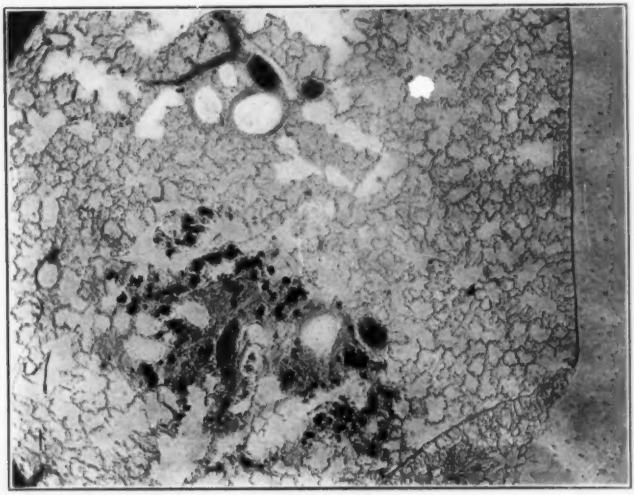


FIG. 6.—Left lung of a rabbit where the mediastinum was injected with India ink.

pigs, rabbits, and sheep were employed. Guinea-pigs and rabbits are known to have very thin pleura and poorly developed septa of

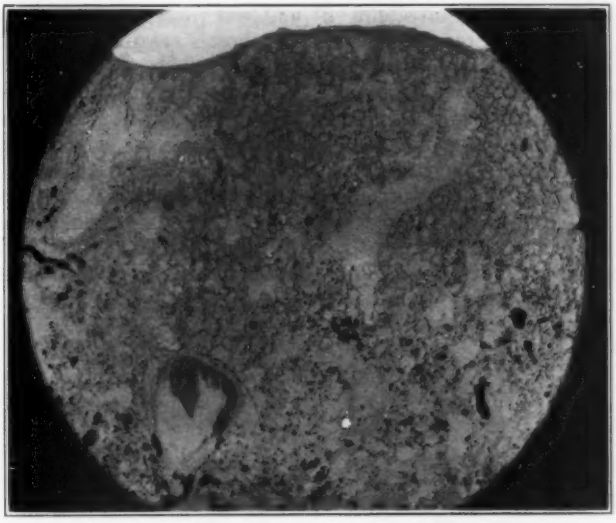


FIG. 7.—Right lung of the rabbit described in Fig. 6.

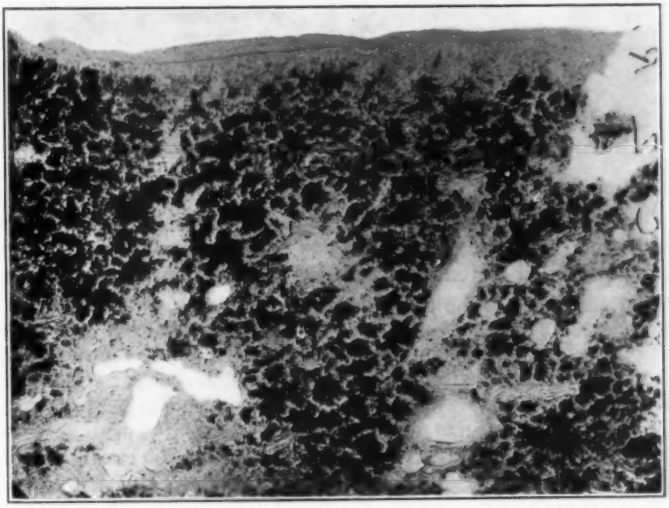


FIG. 8.—Right lung of a rabbit where the right pleural cavity had been injected with India ink. Showing large quantities of India ink throughout the lung structure.

the secondary lobules. Sheep, on the other hand, have a thick pleura and well developed septa, very similar to those conditions found in the human lung. The first set of investigations was to determine the transmissibility of material from the mediastinum into the lung substance. The material chosen was, during the early investigation, an aqueous suspension of charcoal. This was found to wash out of the tissues during the process of staining and in that way prevented a microscopical study of its distribution, consequently its use was given up and in its place India ink, which proved most satisfactory and permits of microscopical study after staining, was employed. Chinese vermilion was also employed in some experiments, but was abandoned because it produced such violent local reactions as to interfere greatly with normal local function. After numerous attempts it was found possible to inject a small quantity

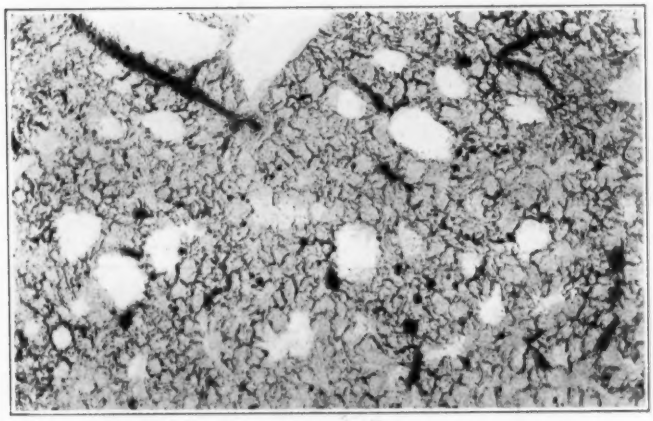


FIG. 9.—The left lung of the rabbit described in Fig. 8.

of material into the mediastinum at the bifurcation of the trachea —thus placing the material in contact with the lung hilum.

The injection of India ink into the mediastinum in this fashion represented the first complete set of investigations and for this purpose guinea-pigs, rabbits, and sheep were employed. A series of guinea-pigs were taken and one-fourth of a cubic centimeter of India ink was injected into the mediastinum once each week for six weeks and the animals autopsied two weeks after the last injection. One-half cubic centimeter was used for the rabbits and they were autopsied four weeks after the sixth weekly injection. For the sheep, about 2 cc were employed and the autopsies were performed six weeks after the sixth weekly injection. The longer time given to the rabbits and sheep after the last injection was an arbitrary decision, as was also the amount of material used. It was thought

to be the part of wisdom to employ larger amounts of materials and to permit a longer time to elapse between the final injection and the autopsy in the sheep and rabbits because of the thick pleura known to be present in these animals and because of their greater size. Following the autopsy, a gross and microscopical study was made of the lungs, thoracic wall, heart, diaphragm, and the tissues of the neck, liver and spleen. In the examination a careful search was made for the presence of the injected material in the tissues, its distribution, and its tendency to collect in masses. All of the animals guinea-pigs, rabbits and sheep, revealed the same findings, which were as follows: There was pigment scattered throughout each lung. This pigment revealed a strong pleural drift, with at places large collections beneath the pleura. Within the lung tissue the greater quantity of the pigment was in the intercellular spaces and in the spaces around the bloodvessels and bronchi, a small quantity being found in those cells called macrophages. There were large collections of pigment within the parietal pleura on each side, but notably none beneath the diaphragmatic pleura and none in the liver or spleen. The same gross findings were present in those animals upon which a suspension of charcoal was used; but, as stated previously, a microscopical study of the tissues for the charcoal is impossible because it is removed by staining.

The result of these experiments proved that pigment, such as India ink or charcoal, can pass from the mediastinum into the lung substance and into the spaces beneath the parietal pleura.

For the second part of the investigation, another series of guinea-pigs, rabbits and sheep were taken and the same quantity of material with the same time intervals as was used in the mediastinum cases was again employed, the site of the injection in these cases being the right pleural cavity, due precaution being taken that the lung tissue was not injured. After the autopsies in these cases a search for the pigment, grossly and microscopically, was made as in the mediastinum cases. Again it was found that the pigment was scattered throughout each lung, the quantity in the left lung being as great as that in the right. The distribution was similar in all respects to that found in the mediastinum cases. The pigment was found in the tissues of the mediastinum and beneath the parietal pleura on each side. Again no pigment was found beneath the diaphragmatic pleura or in the liver or spleen. The findings were the same in all three types of animals; and, as before, those cases where charcoal was employed revealed the same general, gross distribution of charcoal as did the others of the India ink.

The results of this experiment indicated that India ink or an aqueous suspension of charcoal placed in the right pleural cavity can migrate throughout the right lung, into the mediastinal tissues, throughout the left lung, and into the subpleural spaces of the parietal pleural.

It is altogether probable that bacteria can thus migrate from one portion of the lung to other parts and even into the opposite lung.

Studying the stained specimens with a high-power lens one can see that most of the pigment found in the lung tissues lies in the intercellular spaces and in the spaces around the bloodvessels and the bronchi. None is observed within the large lymph trunks or the bloodvessels and a very small portion, relatively, in the macrophages.

I cannot close the discussion of this experimental work without acknowledging my great indebtedness and gratitude to Sister M. Florina, Chief of the Laboratories of St. Anthony's Hospital. Her assistance was invaluable in sectioning and staining the tissues.

Summary. The observation herein described demonstrates beyond question that rather coarse material, such as an aqueous suspension of charcoal, can through some pathways migrate from one portion of the thoracic cavity to another portion and throughout the respiratory tissues. The mechanism of this migration depends probably more upon the physiology of the pulmonary respiration with the almost constant movement of the intrapulmonary fluids than upon phagocytosis or lymph flow as it was formerly conceived. This phase of the question is still under investigation in our laboratories and the results of that investigation will be forthcoming.

In succeeding discussions we shall attempt to show the influence of the reticulo-endothelial system upon the distribution of the pigment.

A NEW VASCULAR SIGN OF DEATH.

By Morris H. Kahn, M.A., M.D.,
NEW YORK.

(From the Department of Cardio-vascular Diseases, Beth Israel Hospital, New York City.)

Although the transition from life to death is a gradual process, certain phenomena take place so definitely at the borderline that we consider them as signs of death.

The phenomenon that I wish to point out as a significant sign of death consists of certain changes in the appearance of the small vessels, especially the veins, all over the body. To speak of these as capillaries would not be consistent with the facts in human beings if we limit capillaries to only those vessels of such small caliber as will admit red blood cells to pass through in single file.

It is the circulatory changes alone that so significantly and so promptly give undeniable evidence of death. Normally, the small vessels are constantly filled, with slight variations in volume as the result of pulsation. Postmortem, the column of blood in the vessels,

sustained and solid, undergoes a change which manifests itself within a limited time.

This change consists of the formation of transverse interruptions in the red color of the vessels, giving the appearance of division or striation of the blood column. These interruptions, often only few in number, are apparently chiefly in the veins and occur both near the disc and distant from it. They occur less constantly in the smaller arteries. While looking at the fundus of the eye, or during the course of frequent repeated examinations of it, or at any accessible superficial venules, one notices from time to time, a distinct variation in the length of one or the other striation. This can be made more evident by turning the head of the subject from side to side or by compressing the vessel momentarily. It can be still more accentuated by pressure upon the eyeball, in both these ways modifying the retinal intravascular pressure. Firm external pressure upon the eye empties the veins in the region of the disc and also the central artery. Upon relaxation the vessels refill to their former capacity. These manipulations for a time after death alter the size of the interruptions considerably. After about one hour no spontaneous alterations in size are noticeable. After a longer time, *i. e.*, about three hours, the vascular striations are no longer influenced by manipulation and pressure. These phenomena are sometimes more manifest in one eye than in the other. These observations have since been confirmed by animal experiments and present a physiological basis for their occurrence.[1]

When the animal dies, the movement of blood in the smaller vessels and capillaries at first comes to a sudden stop. Then the corpuscles clump slightly and shortly begin to move forward in the normal direction. This movement, at first noticeable in the capillaries, extends to the venules and there is a slow and gradual progression of blood toward the larger veins. The appearance is as if no blood entered the capillaries from the arterial side and that a milking process, akin to peristalsis, swept the corpuscles onward toward the vein. When the process is complete it may be found that here and there in the capillary net a few clumped corpuscles are locked as if the constriction of the vessel had failed to carry on the last of its contents.

These changes occupy varying lengths of time in different animals. They may develop completely in a few minutes or they may last half an hour or more. The completeness with which the vessels empty is also a varying factor. Sometimes, particularly in old and debilitated animals, the blood may not be moved at all; sometimes the field is swept absolutely free of blood but more often a few clumps of corpuscles are left stranded, particularly in the venules. The stagnation of these clumped corpuscles is the significant feature which I consider the early appearing sign of death.

[1] Hooker, D. R.: Am. Jour. Physiol., 1920, **54**, 30.

That these events are not alone evidences of peripheral changes in the circulation but also central may be shown by the fact that in a large portion of human dying hearts, the venous ends, that is the auricles, continue to beat for a long time after the ventricles, and in that way effect changes in the peripheral circulation, especially in the venules.

It is known that blood remains uncoagulated for a long period inside of uninjured bloodvessels. Finally, of course, intravascular coagulation takes place. Segmentary in occurrence with consequent shrinking of the fibrin, this leads to the formation of intercoagular spaces containing serum. The clots in the vessels contract, and thus separate in places from each other, leaving between them the serum which is expressed in the process of congealing. In a number of cases the intercoagular intervals were not observed. In these cases, probably clotting of the distal arterial column took place *en masse;* and the serum that otherwise formed the intercoagular interval, was expressed murally. In a few of the cases presenting choked discs no intercoagular intervals were found. Here the above-enunciated explanation is the more maintainable, drawing support from the idea that the central pressure favored coagulation *en masse.* It is likely that it is the adherance of the fibrin to the vessel wall that finally prohibits variation by pressure, of the size of the intercoagular spaces.

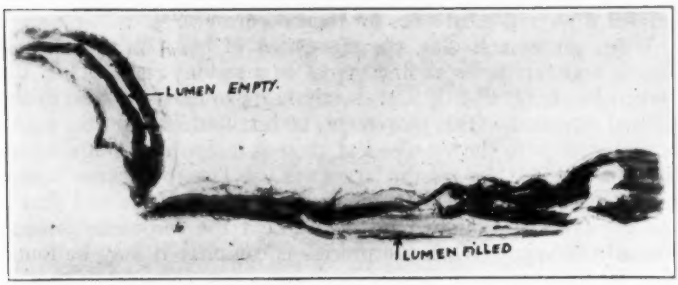


FIG. 1.—Longitudinal section of an arteriole showing the filled segment and another part empty of blood corresponding to the intersection.

An obvious analogy applies when we consider clotting in the large vessels of the trunk. On examination of these, the clots are found to be, so to speak, in segments, with serum in the intervals. (Fig. 1). When one carefully observes the peritoneal surface of the intestine postmortem or after resection, he may see that the small vessels, chiefly the venous radicals, present the interruptions corresponding to the intercoagular spaces. This appearance, due to intravascular clotting, may be found intravitam in embolism or thrombosis of the mesenteric vessels.

In vitro, segmentary coagulation can be produced, but not without difficulty. Given the conditions comparable to those existing in small vessels, the blood clots usually with the expression of serum along the wall, not with the formation of intercoagular spaces. We made use of capillary glass tubes. I tested this repeatedly with normal and abnormal blood in several cases of delayed coagulability with jaundice, and in one case of hemophilia in which fibrin showed itself only nineteen minutes after the blood was drawn. Lowering or raising the temperature of one part of the tube was of no influence. In the tubes in which the blood was allowed to flow in with interspaces of air, however, there was often intercoagular lodgment of the serum. When the glass capillary tubes were filled completely with a rapidly coagulable blood, the ends then sealed with paraffin, and the tubes suspended vertically, the irregular shrinking of the fibrin gave the appearance of segmentary coagulation. (Fig. 2.)

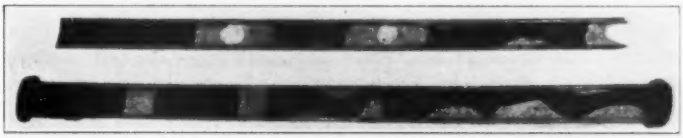


FIG. 2.—Segmentary coagulation *in vitro*.

A diligent perusal of the recent literature on ophthalmoscopy and the recognized signs of death revealed no mention of the occurrence postmortem of their segmentary appearance except in my previous studies of the subject.[2]

Conclusion. That segmentation of the venules and arterioles is a definite sign of death is an established fact and it should be ranked equally with the other clinical signs of death.

AURICULAR FLUTTER, WITH PERIODS OF 1:1 VENTRICULAR RESPONSE.

BY THOMAS M. MCMILLAN,

AND

JOHN A. SWEENEY,

PHILADELPHIA.

(From the Department of Cardiology of the Laboratories of the Philadelphia General Hospital, Philadelphia, Pa.)

IN the vast majority of cases flutter of the auricles is associated with some degree of *A-V* block. Very rarely there may be no block, the ventricles responding to the auricles beat for beat.

[2] Kahn, M. H.: Med. Rec., 1913, **83**, 801; Berl. klin. Wchnschr., 1916, **53**, 1237.

As far as we can find, there are but 10 recorded instances of this mechanism. Instances of this disturbance have been reported by MacKenzie,[1] Lewis,[2] White and Stevens,[3] Koplik,[4] Blackford and Willius[5] (3 cases), Smith[6] and Hewlett.[7] Scott[8] recently published tracings of, and discussed, a case of this disturbance which our case resembles very closely.

A brief history of our case follows:

J. B., a white male, aged fifty-seven years, entered the medical wards of the Philadelphia General Hospital, June 10, 1923, complaining of substernal pain. At its beginning the pain had been intermittent, but about three weeks before admission it became constant, but not particularly severe. There was a history of breathlessness, fatigue on exertion and short attacks of very rapid heart action, during which the patient became very weak and extremely short of breath. These attacks came on suddenly, lasted from three to five minutes and terminated gradually. They always followed some exertion. Aside from nocturia, the rest of the history of the present illness was unimportant. The past history was negative, except for the occurrence of a penile sore ten years previously.

The examination showed a well-nourished man, who did not appear ill. In the chest were found unmistakable signs of an aortic aneurysm, which, it was thought, was the cause of the substernal pain. The heart was little, if at all enlarged; the left base measured 9.5 cm. from the midsternal line and the right 2.5 cm. At the apex could be heard a soft blowing systolic murmur. At the base in the second right interspace was heard a loud harsh systolic murmur followed by a soft blowing diastolic murmur.

The Wassermann test was positive by two antigens. The fluoroscope bore out the clinical diagnosis of aneurysm. The urinary findings were negative in the early stages of his illness, but before death showed large amounts of albumin and varieties of casts.

On admission the pulse-rate was 130. Electrocardiograms showed this to result from auricular flutter with 2 :1 block.

After the studies reported in this paper had been made the flutter was easily abolished by digitalis and a normal mechanism restored. The sinus rhythm continued uninterruptedly until his death, six months later, from an acute tubular nephritis and bronchopneumonia.

Fig. 1 shows tracings from the three customary leads and an additional strip from lead II taken during vagal pressure. This latter maneuver enabled us to see the auricular waves more clearly and to determine definitely that auricular flutter was present with an auricular rate of 260 and a ventricular rate of 130.

We had obtained a history of attacks of very rapid heart action

brought on by exertion. Such an attack was induced on several occasions by having the patient bend forward and then straighten up from three to ten times. The rapid ventricular rate that resulted from this relatively trivial exercise was shown by the electrocardiograph to have resulted from the ventricles responding to every auricular impulse instead of to every second impulse of the fluttering auricle. The auricular rate was unchanged; the ventricular rate was doubled and equalled that of the auricle. The shape and duration of the *Q–R–S* complex was quite the same as

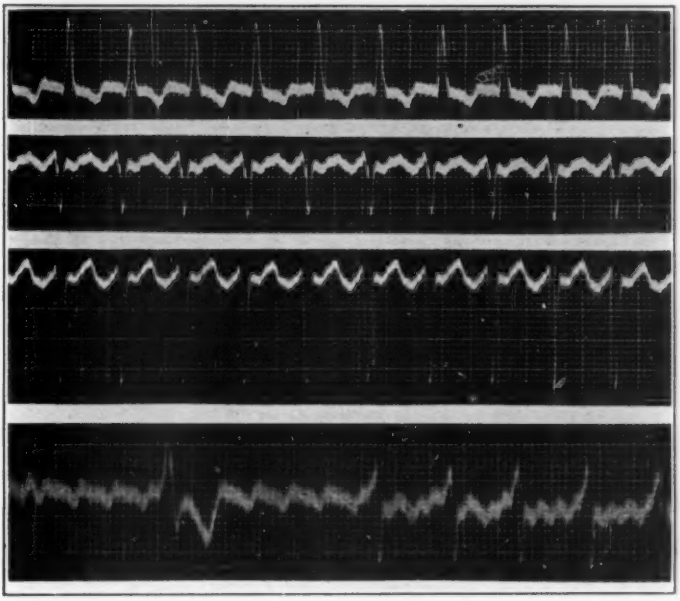


FIG. 1.—The first three strips are from the three customary leads. They show a left ventricular preponderance and auricular flutter with 2:1 block. The lowest tracing is a strip of lead II taken during the application of vagal pressure. This slowed the ventricular rate and showed more clearly the character and rate of the auricular waves. Time in one-fifth and one-twenty-fifth second.

when 2:1 block was present. Figs. 2 and 3 are electrocardiograms obtained during a paroxysm of this 1:1 conduction. These paroxysms of rapid heart action would continue unabated for perhaps three minutes. Irregularities in the ventricular responses could then be noted. In Figs. 2 and 3 it can be seen that these irregularities were due to an occasional failure of the ventricle to respond to an auricular impulse. This failure of response gradually became more pronounced until every third auricular impulse failed to be followed by a ventricular contraction. This type of action soon

gave way to the regular and constant 2:1 ventricular response present before the rapid rate set in. It can be seen in Figs. 2 and 3 that, during the transition stage from 1:1 to 2:1 conduction, the

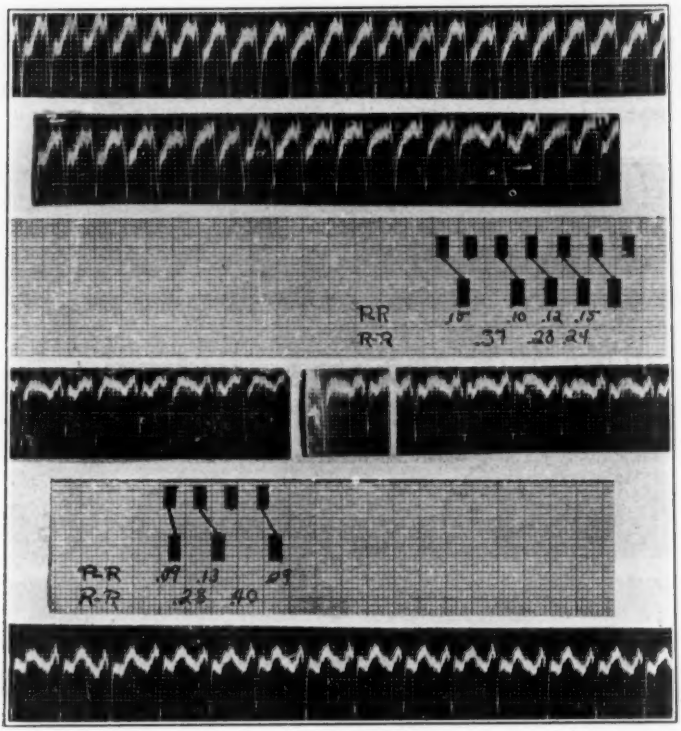


FIG. 2.—The *first strip* shows a paroxysm of 1:1 conduction at its height. The *second strip* is continuous with the first. The first irregularity in the ventricular response to appear is shown toward the right of the tracing. This irregularity is due to failure of the ventricle to respond to an auricular impulse. The *third strip* is a diagram to illustrate the variation of the *P–R* and *R–R* intervals in the preceding record after a failure of ventricular response. The *fourth strip*: Part I shows a further stage in the return to 2:1 conduction. Two successive auricular impulses cause ventricular responses; the third auricular impulse is blocked. Part II is continuous with the first part. The white line signals the beginning of vagal pressure (see text). From this point on 2:1 response is permanent. The *fifth strip* is a diagram to illustrate the behavior of the *P–R* and *R–R* intervals. The *sixth strip* is continuous with the fourth and shows a continuation of the reëstablished 2:1 conduction. Time in one-fifth and one-twenty-fifth second.

actual *A–V* conduction time varies: after a dropped beat the next ventricular response occurs after a shorter *P–R* interval. Where cycles of both 1:1 and 2:1 conduction are seen the differences of *A–V* conduction time in these respective cycles are such that the

R–R interval of a 2 : 1 cycle is considerably less than twice as long as the R–R interval of a 1 : 1 cycle. The cause of this change in A–V conduction time is to be discussed presently.

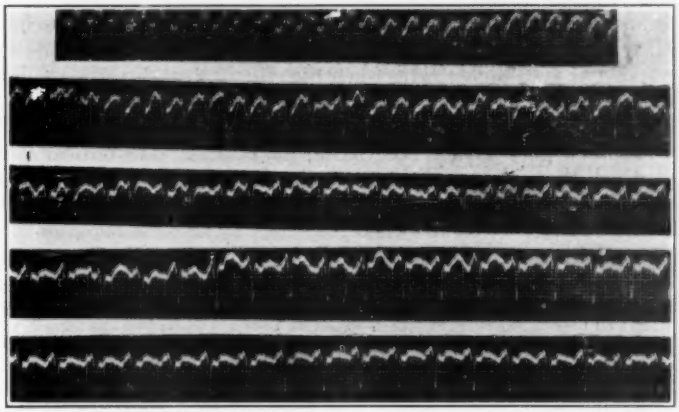


FIG. 3.—This is a continuous tracing of a short paroxysm from the beginning of 1 : 1 conduction to the final restoration of 2 : 1 response. Time in one-fifth and one-twenty-fifth second.

Discussion. *The Cause of the Change from 2 : 1 to 1 : 1 Conduction.* The factor in this case that so suddenly and profoundly modified the rate of ventricular response to auricular impulses was in all probability an alteration in the duration of the refractory period of the muscle of the A–V node. This conclusion is based on deductions made by Lewis[9] from certain of his experiments. He believes that the evidence of these experiments, as well as certain other considerations, points to the conclusion that certain forms of heart-block are finally to be explained in terms of altered excitability of various portions of the cardiac musculature.

That actual dropped ventricular beats result from the muscle of the A–V node being in a refractory state at the time of stimulation is a generally accepted statement; but that delay in conduction results from a state of partial refractoriness was not recognized before Lewis's work. According to Lewis, excitability and conductivity are interdependent and not independent properties of heart muscle.

In studying the effects of rapid stimulation on various structures of the heart, Lewis showed that when a critical rate of stimulation was reached certain abnormalities in the cardiac response occurred. These abnormalities were: (1) A prolonged conduction time of the impulse, and (2) as the rate of stimulation was advanced somewhat, an actual failure of response. The critical rate of stimulation beyond which these abnormalities occurred varied for different portions of the

heart. In the case of the *A–V* node prolonged conduction occurred at rates of 272 to 300 per minute. When this structure was stimulated by auricular impulses at rates higher than this critical level the ventricle would respond only to every second impulse. This failure of ventricular response was in no way due to lack of excitability of the ventricular muscle, for the ventricle could be made to respond at even higher rates when the stimuli were directly applied to this structure. The site of the block was evidently the *A–V* node.

A similar phenomenon occurred in the auricle. The critical rate at which these abnormalities of conduction occurred lay, however, at a higher level.

The cause of these abnormal responses to rapid stimulation by the auricle was found by a study of the effect of vagal stimulation. Lewis showed that when prolonged conduction, or even 2 : 1 response, was occurring in an auricle being stimulated at a rate above the critical level, vagal stimulation would abolish both these abnormalities of conduction. His conclusions were that the 2 : 1 response resulted from the muscle being completely refractory at the time of each second stimulation. The state of prolonged conduction time that preceded 2 : 1 response resulted from the muscle being partially refractory. In finding excitable fibers under these conditions the impulse had to pursue a circuitous path, and thus prolonged the time of conduction. There was no change in the actual rate of fiber conduction. Vagal stimulation abolished these abnormalities by shortening systole and thus shortening the refractory period by increasing the time for the recovery of excitability.

In the case of the *A–V* node vagal stimulation had no such effect in abolishing delayed conduction or 2 : 1 response; it increased the block. Rather than believe that vagal stimulation has a fundamentally different effect on the muscle of the auricle and node, Lewis formulated the hypothesis that vagal stimulation has two effects on the muscle of these two structures. The first effect is a shortening of the length of systole. This allows recovery to begin earlier, and thus assures a quicker return of excitability. The second vagal effect is a decrease in the rate of the recovery process. In the case of the auricle the first vagal effect predominates, whereas in the *A–V* node the second effect predominates. Thus Lewis explains the differences seen in the two structures on vagal stimulation.

If we accept Lewis' explanation of these phenomena,* we can say of the case reported here that: (1) The periods of 2 : 1 ventricular response resulted from the muscle of the *A–V* node being completely refractory to every second auricular impulse; (2) that the periods of 1 : 1 response following exercise resulted from a lessening

* This explanation has been discussed by Scott (loc. cit.)

of the refractory state of the muscle or at least of some of the fibers; (3) that the prolonged P–R intervals seen during 1:1 conduction resulted from the impulse having to traverse a circuitous path due to the muscle of the A–V node being partially refractory.

As to what process caused the sudden change in the excitability of the A–V node in this case we can only surmise. We can only say with certainty that the change followed exertion. The effects of exercise on the heart are complex. Release of vagal tone is certainly one of the most conspicuous. According to the hypothesis of Lewis cited above, this latter reaction might bring about the periods of 1:1 conduction by speeding the rate of recovery of excitability. Considerable light could have been thrown on the relation of vagal inhibition to the onset of these paroxysms of 1:1

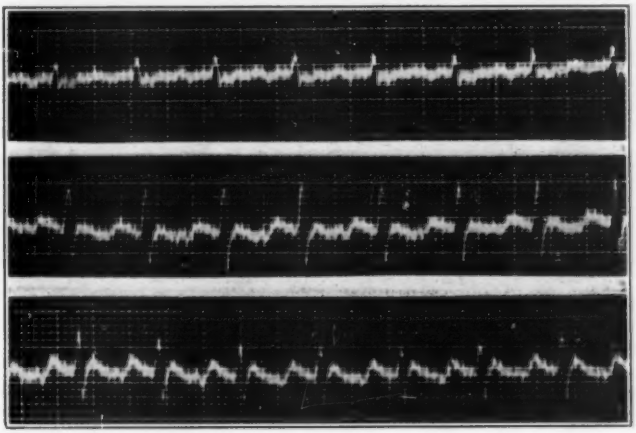


FIG. 4.—Case II. A tracing showing auricular flutter with 2:1 block. Time in one-fifth and one-twenty-fifth second.

conduction could we but have induced such a response by atropin or ended a paroxysm by vagal stimulation. We dared not make the atropin study because of the severe effects on the circulation of these paroxysms. The effect of vagal pressure, as we observed it when applied during the periods of 1:1 conduction, was to increase the degree of block. In Fig. 2 is shown the effect of vagal pressure applied while alternating cycles of 1:1 and 2:1 conduction were occurring. The spontaneous changes in conduction occurred so rapidly, however, that we do not feel that we can speak positively of this reaction.

The Circulatory Response to the Rapid Ventricular Rate. The effects of a tachycardia, such as this case exhibited, depend on many individual factors. In the case we are reporting, while 2:1 con-

duction and a ventricular rate of 130 was present, there was little or no embarrassment. With the onset of 1:1 conduction, however, the circulatory distress became extreme. Fortunately the paroxysms were of short duration.

The Frequency of Periods of 1:1 Conduction during Auricular Flutter. The scarcity of reported cases of this mechanism would indicate that it occurs but rarely. It is our impression, however, that this disturbance occurs more frequently than the number of reported cases indicate. This impression is strengthened by our having obtained a history strongly suggestive of this disturbance in

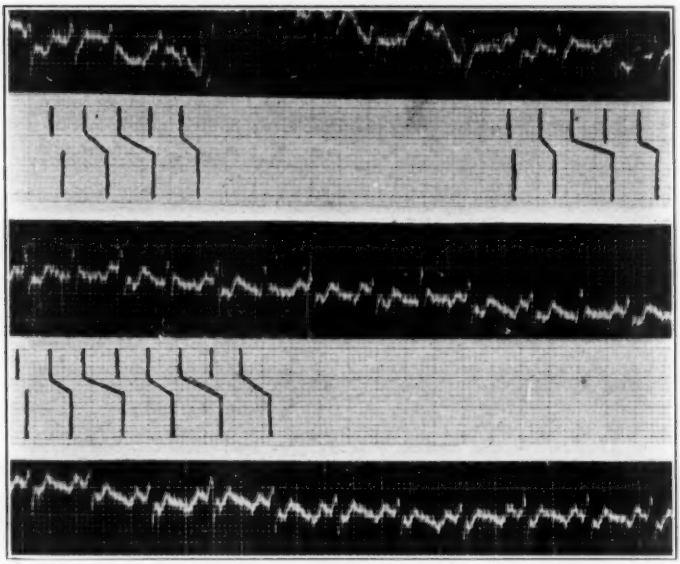


FIG. 5.—Case II. A continuous tracing of lead II taken after moderate exertion. For a time, as shown in the diagrams, the ventricle responded to two successive auricular impulses, each third auricular impulse being blocked. Time in one-fifth and one-twenty-fifth second.

several other cases of auricular flutter. Since the case reported here came to our attention, we have had but one other case of auricular flutter on which it seemed safe to attempt to induce 1:1 conduction. In this second case, hopping ten times on each foot brought on a 3:2 response for a time, that is, there were alternate cycles of 2:1 and 1:1 conduction. Figs. 4 and 5 are examples of this mechanism.

Summary. A single case of auricular flutter is reported in which the ordinarily present 2:1 block was interrupted by periods of 1:1 conduction, which lasted two to three minutes. These paroxysms

were very easily induced by relatively slight exertion. When present these paroxysms placed a serious and alarming strain on the heart.

A second case of auricular flutter is reported in which exertion brought on 1:1 conduction in alternate cycles.

It is suggested that periods of 1:1 conduction in auricular flutter are more common occurrences than the scarcity of reported cases would indicate.

BIBLIOGRAPHY.

1. MacKenzie, Sir J.: Diseases of the Heart, 3d edition, Oxford Medical Publications, London, 1913.
2. Lewis, Sir T.: Lectures on the Heart, Paul B. Hoeber, New York, 1915.
3. White, P. D., and Stevens, H. W.: Arch. Int. Med., 1916, **18**, 712.
4. Koplik, H.: Am. Jour. Med. Sci., 1917, **154**, 834.
5. Blackford, J. M., and Willius, F. A.: Arch. Int. Med., 1918, **21**, 147.
6. Smith, S. C.: Heart Records; Their Interpretation and Preparation, F. A. Davis Company, Philadelphia, 1923.
7. Hewlett, A. W.: Pathological Physiology of Internal Diseases, D. Appleton & Co., New York, 1923.
8. Scott, R. W.: Jour. Am. Med. Assn., 1922, **79**, 1984.
9. Lewis, Sir T.: Quart. Jour. Med., 1921, **14**, 339.

REVIEWS.

HANDBOOK OF SKIN DISEASES. By FREDERICK GARDINER, M.D., Lecturer on Skin Diseases, University of Edinburgh. Second edition. Pp. 248; 46 figures and 12 colored plates. New York: William Wood & Co., 1924.

THIS pocket-manual is in the quiz-compend class, and while designed for students lacks the concise, categorical characters that make American counterparts so valuable in a crowded curriculum, and which it cannot hope to replace. The illustrations are not bad; binding, printing and quality of paper are good; but the price of this small handbook is quite in keeping with the excessive prices of English medical books in general. W.

THE FIRST CENTURY OF THE PHILADELPHIA COLLEGE OF PHARMACY. Edited by JOSEPH W. ENGLAND. Pp. 728; illustrated. Philadelphia: Philadelphia College of Pharmacy and Science, 1924.

THIS splendid book is a very complete history of the College of Pharmacy in the past hundred years. It contains a most interesting mass of historical data which should be of great interest to anyone connected with the College and of interest to medical and pharmaceutical historians. The book is beautifully prepared, very well gotten up and is a tome which redounds to the credit of the editor and editorial board. M.

INSULIN IN GENERAL PRACTICE. By A. CLARKE BEGG, M.D. O.B.E., CH.B., M.B., Honorary Physician to Swansea Hospital, London. Pp. 130; 4 illustrations. London: William Heinemann, 1924.

THIS is the third or fourth book that the reviewer has had the opportunity of seeing which deals with specific directions to the practitioner for the care of the diabetic, and more particularly with

the use of insulin. It is, however, the first that has come from England, therefore it is not necessarily an addition to an already overcrowded literature but rather is a book prepared for the practitioners of another country. It compares most favorably with those which have been prepared in the United States and in some respects is probably superior to any we have seen. On the whole, however, the little books on insulin therapy are very much of the same general type and are all equally good. M.

THE MEDICAL DEPARTMENT OF THE UNITED STATES ARMY IN THE WORLD WAR. Volume XI. Surgery. Part Two. Pp. 827; illustrated. Washington: Government Printing Office, 1924.

THIS third volume of the Medical Department of the United States Army in the World War which has just appeared is fully up to the standard of the two which have preceded it; indeed I might say that it is superior from the surgical standpoint though not historically as important as the other two volumes. This volume deals with empyema, maxillofacial surgery, ophthalmology in the United States and in the A. E. F., and otolaryngology in the United States and in the A. E. F. These various sections are very well presented and profusely illustrated. The colored photographs of the lungs are beautiful examples of the printer's art. The first three sections of the book are particularly commendable, the last three are hardly as complete as the first three sections. If the succeeding volumes of the history of the Medical Department in the World War are as well executed as this present volume a tremendous amount of valuable information will be available for the medical profession and for medical officers. M.

THE FOUNDATION OF HEALTH. By WILLIAM BARNARD SHARP, S.M., M.D., PH.D., Professor of Bacteriology and Preventive Medicine in the Medical Department of the University of Texas. Pp. 256; 20 illustrations. Philadelphia: Lea & Febiger, 1924.

THE *Foundation of Health* is a physiology for the layman and more particularly the lay student who wishes to know about the various bodily processes which take place in daily life. It deals largely with physiology, with an added atmosphere of anatomy and personal hygiene, the parts melded together into a complete whole which presents a most thorough and complete exposition of what the individual should know about his own body and about the care of the body. A book of this type is hard to prepare to bring it down

to the level of the non-medical reader so that he can understand and comprehend it. The author has done this so successfully that the book can be recommended to anyone who is interested, and most of us are, in the body and personal hygiene. M.

THE HUMAN TESTIS AND ITS DISEASES. By MAX THOREK, M.D., Surgeon-in-chief, American Hospital; Consulting Surgeon, Cook County Hospital, Chicago, Ill. Pp. 548; 308 illustrations. Philadelphia: J. B. Lippincott Company, 1924.

A MOST interesting book and a title that makes one hope that a true successor to Curling has appeared. One quickly perceives, however, that the author's interest centers in the endocrinology of testicular function and the subject matter relative to true pathologic conditions is woefully relegated into a minority role, frequently discharged with extensive quotations from other authors or simply sparingly treated. That the subject of hydrocele in its entirety can be dismissed with a scant 125 lines; or that vaso-epididymal anastomosis in sterility demands only 28 lines (with no mention of Hagner's work); or that epididymitis can be dismissed with an inheritance of the last four pages of this large book, shows that the volume is poorly balanced and does not represent its title. When the author writes on his special forte and simply deals with the physiological functions, normal and perverted, the book constitutes an excellent presentation of the mass of recent literature on the subject of gonadal endocrinology, which is fairly presented, carefully analyzed and judiciously passed upon, and likewise enhanced by the author's valuable work on transplantations. On this side of the subject it represents a valuable milestone in advancing medicine. R.

A RECORD OF MEASUREMENTS, WEIGHTS, AND OTHER FACTS RELATING TO MAN. THE WILLIAM RAMSEY HENDERSON TRUST REPORTS NOS. 2 AND 3. By J. F. TOCHER. Pp. 172. Edinburgh and London: Oliver and Boyd, 1924.

THIS volume constitutes the second and third of the Henderson Trust Reports, the first having been published in 1905. It consists of anthropometric observations on samples of the civil populations of Aberdeenshire, Banffshire and Kincardineshire, and a study of the chief physical characters of soldiers of Scottish nationality and a comparison with the physical characters of the insane population of Scotland. A.

MODERN METHODS OF TREATMENT. By LOGAN CLENDENING, M.D., Assistant Professor of Medicine, Lecturer on Therapeutics, Medical Department of the University of Kansas. Pp. 692; 77 illustrations. St. Louis: The C. V. Mosby Company, 1924.

THE purpose of this book, according to the author, is "to present a comprehensive statement of the best modern thought and practice upon the treatment of diseases included in the general specialty of internal medicine." "A book on treatment," he continues, "should give a method of procedure so clearly and minutely that a person who has never heard of it could do it from the description." The pages which follow admirably carry out these ideas. Approximately one-quarter of the book is devoted to instruction in the use of important drugs; unimportant ones are omitted. One-third of the work describes the application of therapeutics to particular diseases. The remainder is devoted to the consideration of special methods of treatment, such as biologic therapy, dietetics, mechanotherapy and radiotherapy. The brief chapter on psychotherapy is especially worth reading. The book will commend itself to practitioners of internal medicine, medical students, and perhaps most of all to hospital interns, who will find included in its pages excellent descriptions of practically all of the therapeutic measures practised in the medical wards of the modern hospital. A.

THE ROMANCE OF A LIVING TEMPLE: A STUDY OF THE HUMAN BODY By FREDERICK M. ROSSITER, B.S., M.D., L.C.R.P., M.R.C. Pp. 254. London and New York: George Sully & Co., 1924.

THE object of this work, as stated in the author's preface, is to arouse in the young a deeper interest in the study of the human body and to instil a "practical knowledge of the physical basis of happiness and morality. The teacher who can create in the young mind a love for the laws of health has accomplished a mighty work in preventive medicine. To regard the body as a temple is not vital, but to see the bearing of practical physiology and hygiene upon yourself is of the greatest importance."

To these ends Dr. Rossiter uses an extended simile of workers erecting a building, stress being laid upon the materials employed and upon the care bestowed on the welfare of the "workers," represented by the various physiological functions.

Dr. Rossiter's simplicity of style and wealth of apt illustration are especially valuable in Chapters 31 to 37 inclusive, which treat of diet. Without discussing the accuracy of all statements made, the average lay reader will probably gather from the book, as a net impression, a focussing of his attention, by means of its novel style,

upon the folly of neglecting the primary laws of health, and in this respect, as the book is eminently readable, its measure of value may be not inconsiderable. W.

GENERAL CYTOLOGY. Edited by E. V. COWDRY, formerly Professor of Anatomy at Union Medical College, Peking, China: Member of the Staff of the Rockefeller Institute for Medical Research. Pp. 754; illustrated. Chicago: University of Chicago Press, 1924.

THIS volume is the result of the combined efforts of thirteen scientists each writing of that phase of cytology most intimately related to his own field. It shares, therefore, the advantages and disadvantages inherent to this type of composite presentation. A variation of excellence is one of the disadvantages and it is evident in the present work. While most of the sections deserve the highest praise and are the most authoritative statements on their subjects today, especially perhaps those by Conklin, McClung, Cowdry and Jacobs, that on the Chemistry of Cells is so inferior as to seriously mar the value of the volume. Phrases such as on page 22—"For all practical purposes, however, the ether which we have called space and time may be referred to as Infinity and Eternity"—seem out of place in a work of this character; nor does a loose statement such as on page 48, "In its (iron's) absence hemoglobin cannot be formed and the disease known as chlorosis is the result."

The other sections, however, make the book invaluable to the worker in this field, although it is scarcely digestible by the undergraduate student. The volume is beautifully prepared and illustrated. An unimportant typographical error on page 4, and on page 367 a transformation of Archives of Internal Medicine into "Arch. Internat. de méd.," suggest the need of some revision. P.

ARTIFICIAL LIMBS: APPLIANCES FOR THE DISABLED. By DR. FLORENT MARTIN, Director of the Technical and Scientific Institute of Artificial Limb Fitting, Brussels. Geneva: International Labor Office, 1924.

THE International Labor Office publishes this volume with the desire to be of service to all persons disabled either in war or in industry. The reasons for its publication may be given in a few words. Its object is the general dissemination of information, and it is therefore not purely scientific in character. It is intended to present information to all those who for any reason are interested in artificial appliances; disabled soldiers or sailors, persons injured

in industrial accidents, institutions for insurance against accidents, invalidity, sickness, etc. It should provide anyone who wishes to obtain an artificial appliance for any given mutilation with precise data as to the conditions which should be fulfilled by any satisfactory appliance, and the best types of limb manufactured in the different countries.

After summarizing the general principles on which surgical and orthopedic treatment of amputations should be based, the author reviews the appliances at present in use, classifying them according to the type of amputation and the method of artificial limb manufacture. He draws attention to those applicances only which are of real and demonstrated practical value and has deliberately omitted experiments in limb manufacture. A brief description is given of each limb mentioned, accompanied by a sketch or photograph and a critical appreciation, so that the reader may be in a position to form an objective opinion. E.

CLINICAL ASPECTS OF THE ELECTROCARDIOGRAM. By HAROLD R. B. PARDEE, M.D., Associate in Medicine, Cornell University Medical School. Pp. 222; 56 illustrations. New York: Paul B. Hoeber, 1924.

THERE have been published recently a number of books for beginners in electrocardiography. Of these Dr. Pardee's stands out as the most interesting, since he has not hesitated to incorporate his own experience and opinions. It is not surprising, therefore, that the book has some of the faults that accompany this outstanding virtue, but they are of minor importance. The style is simple and direct and the thought clearly expressed. The discussion of the various aspects of electrocardiography is adequate for the most part to serve as an introduction to the subject. An excellent case is made out for the clinical use of the electrocardiograph. W.

DISEASES OF THE EYE. By CHARLES H. MAY, M.D., Director and Visiting Surgeon, Eye Service, Bellevue Hospital, New York. Eleventh edition. Pp. 445; 374 illustrations. New York: William Wood & Co., 1924.

THIS handbook is admirably arranged for students and practitioners, although it is not intended to replace the larger text-books of reference.

Each chapter commences with an anatomical and physiological review of that part of the eye to be discussed, which is a distinct asset in studying the different diseases of the eye and its adenexia.

The chapters on Uveitis and Disturbances of Motility have been rewritten. The size of the book has not been enlarged, though in its revision it has been brought up to date. S.

PROTOPLASMIC ACTION AND NERVOUS ACTION. By RALPH S. LILLIE, Professor of General Physiology, University of Chicago. Pp. 417; 6 illustrations. Chicago: The University of Chicago Press, 1923.

THIS is a discussion of the fundamental properties of living matter, from the physicochemical point of view. The chief distinguishing characters of organisms are growth, development and an integrative correlation of activities. The essential problem in the physiology of growth is that of the conditions of specific synthesis in protoplasm, and the problem of integration resolves itself largely into the study of the conditions under which protoplasmic processes, although spatially separated, mutually influence one another, *i. e.*, the problem of transmission. To the solution of these questions the author has made valuable contributions, one of the more recent of these being the study of chemical transmission along an iron wire immersed in nitric acid. He has been able to show in some detail the parallels between the transmission of these chemical effects in the inorganic model and the transmission of nerve impulses in living nerves. He has also devoted much time to the study of cellwalls as semipermeable membranes and the relation of their properties to anesthesia and metabolism. In this book he has brought together and reviewed his results, thus giving a collected discussion of these fundamental but intricate processes of life.

A.

ANESTHESIA IN DENTAL SURGERY. By the late THOMAS D. LUKE, M.D., F.R.C.S. (EDIN.). Edited by J. STUART ROSS, M.D., F.R.C.S. (EDIN.), Honorary Anesthetist, Edinburgh Dental Hospital, and Lecturer in Anesthetics, Edinburgh University. Fifth edition. Pp. 238; 45 illustrations. London: William Heinemann, 1924.

THE fact that this is the fifth edition is proof of the popularity of the book in Great Britain. The first chapter is a very complete history of anesthesia. The authors indicate a marked preference for general anesthetics in dental surgery, and give an excellent presentation of nitrous oxide, ethyl chloride, ether and chloroform as adapted to this field. The chapter on local anesthesia is inadequate when measured by the standards of American practice.

I.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

TAYLOR PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO.

Exsanguination-transfusion, A New Therapeutic Measure in the Treatment of Severe Toxemias. — ROBERTSON (*Arch. Surg.*, 1924, **9**, 1) as a result of his extensive experience in treating the various toxemias of children, has come to place great reliance on the operation of exsanguination-transfusion. The technic calls for replacing all, or nearly all, of the patient's blood by the blood of donors, so that the method is necessarily limited in its application to children because of the difficulty of obtaining sufficient donors for larger patients. Several donors are always prepared and at hand before the operation is started even on a child. Best results have been obtained when practically the whole of the child's blood is replaced. Blood is drawn from the donors, citrated to 0.35 per cent, and kept at body temperature until needed for injection. The child is bled from the superior longitudinal sinus in case the fontanelle is still open, otherwise from the superficial veins. When exsanguination has proceeded to the point where the pulse begins to weaken, the injection of the donors' blood is begun. Thereafter the two processes go on simultaneously. To date (March, 1924), the operation has been repeated on 501 occasions, with increasingly beneficial effects. Best results are seen in children suffering from the toxemias of severe superficial burns, erysipelas, acute septic scarlet fever, and in acute intestinal intoxication.

The Effect of Iodin in Exophthalmic Goiter. — The definite value of iodin therapy in exophthalmic goiter reported by Plummer from the Mayo Clinic in May, 1923, has since been confirmed and emphasized by PLUMMER and BOOTHBY (*Jour. Iowa Med. Soc.*, 1924, **14**, 66) at the Mayo Clinic and by STARR, WALCOTT, SEGALL and MEANS (*Arch. Int.*

Med., 1924, **34**, 355) at the Massachusetts General Hospital. The latter group of investigators studied a series of 25 exophthalmic goiter cases treated identically in the hospital. Liquor iodi compositi, U. S. P., was used uniformly, the usual dose being 15 drops daily well diluted in water and taken after meals. Twelve of the 25 patients responded to the iodin therapy with the acute iodin remission resembling the effect produced by subtotal thyroidectomy. Eight others showed remissions of a less extensive degree. Of the 5 cases treated unsuccessfully, 2 of the patients were pregnant and a third had cardiac decompensation. So if the uncomplicated goiter cases treated under iodin, 92 per cent showed marked improvement. In every case, however, where iodin was discontinued, there occurred within one or two weeks a rapid rise in metabolic rate and an increase of toxic symptoms. The important point is made that, if a patient receiving iodin is to be operated upon, the iodin therapy should not be discontinued before the operation on account of the recurrence of symptoms noted above.

The Nasal Accessory Sinuses in Cardiopathies.—Three cases, with autopsy findings, are reported by MILLER (*Arch. Int. Med.*, 1924, **34**, 177) in a preliminary note emphasizing the importance of a careful scrutiny of the nasal accessory sinuses in all cases of vegetative endocarditis. In each of these three cases of acute vegetative endocarditis there was no suspicion of sinus involvement during life, yet at autopsy one or both maxillary sinuses were found to contain pus and to show evidence of rather long-standing infection. He advises thorough investigation of the nasal sinuses in all cases of vegetative endocarditis in the hope that no cases of sinus empyema be overlooked.

The Ex-service Man and His Lungs.—One of the most interesting developments of the war has been the large number of ex-soldiers who have been crippled as a result of infection of the lungs, the majority of cases, at least in the minds of these ex-soldiers, as a result of the inhalation in small quantities of one of the lethal gases. HAWES (*Jour. Am. Med. Assn.*, 1924, **83**, 1490) describes his experience from a study of 1200 such cases. He divides the 1200 cases that he has seen and of which he has accurate records into groups as follows: (1) Tuberculosis, active and inactive; (2) cases wrongly diagnosed as tuberculosis; (3) gas and its complications; (4) influenza and its complications; (5) nontuberculous pulmonary conditions. Of the first group he says tuberculosis is primarily a great diagnostic dumping-ground, and that whereas twenty-five years ago the tendency was to avoid making a diagnosis until the disease was fully fledged, now the pendulum has swung in the other direction and that in these ex-service men the tendency is to describe all symptoms referable to the chest as tuberculous; the great majority of these patients did not have active tuberculosis though many of them have the signs of an inactive lesion. As causes for the wrong diagnoses of tuberculosis he attributes the errors in part to three main divisions: (1) Failure to spend sufficient time in history taking; (2) lack of temperature and pulse records; and (3) overemphasis of the roentgen-ray findings. The causes of error apply not only to the examination of ex-service men but also to the civilian. Hawes also points out that of the 344 cases that were referred to him because of pulmonary

symptoms which were thought to be due to gas, that in only 19 or 5 per cent could he say that gas had been a factor in a subsequent tuberculous process, but on the other hand chronic bronchitis occurred in 147 of these gassed men. The diagnosis of a neurosis was the only one that could be made in 25 per cent of these gassed cases. These figures are particularly interesting because in the mind of the average physician there has developed the idea that gas has been the cause of a great number of pulmonary cripples, and this idea is even more exaggerated in the minds of the laity, whereas the physicians such as Hawes who carefully study these cases and who do come in contact with large numbers of so-called gas cases found that the gases had practically no effect whatsoever on the development of a tuberculous pulmonary process. Certainly the majority of the patients who complain of gas symptoms have the fear of gas and the effects of gas so inculcated in their minds that they attribute all types of awful results to these substances. Tuberculosis of the lung is thought to be present by many of these patients because of the more or less persistent bronchitis associated with coughing, sensation of constriction of the chest and general weakness. These patients in addition to their neurotic symptoms also have the ever present desire to receive large compensation. It has been the reviewer's good fortune to have had the opportunity of following from time to time a half a dozen men who were first seen a comparatively few hours after being gassed. All these men had a widespread pulmonary lesion and were severely gassed. Gradually the pulmonary signs have cleared up, these men were intelligent officers and upon their return to civil life at once began to earn a living and have done so most successfully ever since. Of course, a small number of cases such as this is not sufficiently large from which to draw conclusions, but these men were seen when their pulmonary condition was most active and have been seen steadily ever since.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE MEDICAL SCHOOL AND ASSOCIATE PROFESSOR OF SURGERY IN THE SCHOOL FOR GRADUATES IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

Intra-abdominal Biliary Exclusion from the Intestines—Cholecystitis—Nephrostomy—A New Method.—KAPSINOW, ENGLE and HARVEY, (*Surg. Gynec. and Obst.*, 1924, **39**, 62) say that the principles involved are the anastomosis of the gall-bladder to the pelvis of the right kidney and ligation and division of the common duct. Immediately after the

first stage bile can be found in the urine in varying amounts, but the animals remain at practically the preoperative weight. This method does not allow for determination of the total biliary output, but pigment studies can be made. It insures a biliary fistula free from injection and necessitating none of the inconveniences of dressings or collecting apparatus.

Mortality from Empyema in Children.—LADD and CUTLER (*Surg., Gynec. and Obst.*, 1924, **39**, 429) declare that empyema in children has a moderately high mortality in their experience and in that of every other surgeon who has reported an appreciable number of cases. The mortality is highest during the first year of life. After the eighth year the mortality should be low and in the present series vanished. The next most potent factor in mortality is the type of the infective organism. Streptococcus hemolyticus yields the highest mortality of the common kinds of infection. Avoidance of operation before the pneumonia has resolved is a factor in the low mortality of this series. Intercostal drainage with an attempt to keep the thorax closed around the tube is the operation of choice with streptococcus infection. Rib resection with freeing of pleural adhesions to allow for expansion of the lung is the operation of choice for the vast majority of postpneumonic cases, because it gives lower mortality rates, requires fewer secondary operations and yields better permanent pulmonary function.

Subcutaneous Tenotomy of the Tendon of Achilles.—GALLAND (*Am. Jour. Surg.*, 1924, **38**, 213) says that it is indisputable that the vast majority of tenotomies performed on the heel cord are followed by firm union. There are cases, however, in which the functional results are not entirely satisfactory. In a large proportion of cases, the unsatisfactory result is due to the fact that the gastrocnemius-soleus group is weak. There are some, however, in which the functional failure is due to the method employed in dividing the tendon. The author describes two distinct subcutaneous tenotomies—the oblique subcutaneous tenotomy, which is indicated in all cases of equinus, in which there is no underlying spastic condition, and second—the subcutaneous plastic lengthening of the tendon which is indicated in all spastic cases and in cases in which the equinus is extreme. The amount of lengthening that will be required can be calculated by taking one-third of the distance, which separates the heel from the floor with the foot held in moderate inversion.

Treatment of Bone and Joint Tuberculosis.—BROCKETT (*Jour. Bone and Joint Surg.*, 1924, **6**, 832) state that there is necessity of a definite diagnosis based on all of the recognized methods of value. It is necessary to distinguish an early primary synovial disease, in the stage before the essential articular structures are invaded from a true articular disease in which these essential structures are involved. Methods employed in treatment are not as important as the way in which the chosen method is carried out and different methods of treatment may and should be carried out in the same case for the various methods which have been so strongly advocated, must each possess virtues. The principles of the different agencies and methods must be understood

and what may be accomplished by them, particularly the conservative ones, in order that the case be given the benefit of their influence whenever and as long as it is possible, but not after their usefulness is over.

The Dangers of Unabsorbable Sutures in Gastroenterostomy.—GILL and JONES (*Lancet*, 1924, **207**, 697) believe the suture of choice is chromic or tanned gut. If a gastrojejunal ulcer develops, it should be treated surgically and not medically. Excision should be performed of the original anastomosis and the ulcer and a reconstruction should be done nearer the lesser curvature. Several authors are cited who have given up silk and thread sutures, who have had no incidence of peptic ulcer since abandonment, in favor of catgut. One author, Wright, had records of 13 cases of gastrojejunal ulceration, due to silk suture. Adams recorded the occurrence of a gastrojejunal ulcer three years after anastomies with a silk knot in the center of the ulcer.

Surgery of the Knee-joint.—ALLISON (*Surg., Gynec. and Obst.*, 1294, **39**, 409) says that operations on the knee-joint, which have for their object the restoration of knee-joint function demand for success the careful handling of the tissues and especially the avoidance of injury of the joint cartilages. Operations upon the knee, which have for their object the obliteration of joint function, require a careful removal of joint cartilages. In children this is all that should be done. In certain disease processes, mostly tuberculosis, operation upon the knee offers the one sure method of cure. Ankylosis should be the objective. Especially in acute infections of the knee, operations to clean the joint cavity, or to establish drainage, hold the only promise of conservation of knee-joint function. Functional use of the lower extremity may be well carried out with a stiff strong weight-bearing knee. Functional use of the lower extremity is inhibited or lost if the knee be insecure, painful or partially functioning. The dangers that can come from an insecure knee are not insignificant. The menace that shadows the life of an individual with a tuberculous knee is very real.

Chronic Stenosis of the Duodenum.—RATKOCZI (*Am. Jour. Roentgenol.*, 1924, **12**, 246) state that chronic duodenal stenoses are divided into two groups—persistent and intermittent. Causes of persistent stenoses are adhesions after laparotomy, adhesions due to tuberculosis and peritonitis and tumors of the stomach and pancreas. Causes of intermittent stenoses are movable tumors, pressure of the mesentery or the superior mesenteric artery, reflex spasm resulting from a lesion elsewhere in the gastrointestinal tract. Duodenal stenoses do not belong to diseases of great rarity. The roentgen examination is decisive It has to ascertain whether there is an organic disease in question and whether there exists a motor disorder, both of which justify the intervention of the surgeon.

The Etiology of the Femoral Hernial Sac.—BUCKLEY (*Jour. Brit. Surg.*, 1924, **12**, 60) says that the sac of a femoral hernia is a preformed sac and is not formed contemporaneously with the expulsion of a viscus. There is not sufficient proof that this preformed sac is of congenital origin. The sac is acquired as a result of properitoneal fat being herni-

ated into the thigh, through that naturally weak site in man—the crural ring. This hernia of properitoneal fat drags with it a small peritoneal sac. Anatomically a man is as much liable to a femoral hernia as a woman. The greater frequency of the condition in women is due to pregnancy and to the prolonged period of raised intra-abdominal pressure, which that condition produces. No existing theory accounts for the fact that among the comparatively few cases which occur below the age of fifteen years, female have a two to one majority.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

NEW YORK.

Contraindications to the Use of Digitalis in Certain Types of Cardiac Insufficiency.—BOEDET and YACOEL (*Arch. de mal. du coeur.*, 1294, **6**, 335) report 3 similar cases of cardiac insufficiency having aortic involvement of different degrees, regular and slow pulse, positive blood Wassermann, and subject to attacks of angina. In each case the angina was aggravated or precipitated by digitalis therapy while intravenous injections of ouabain caused relief of symptoms. Clinical examination during the acute attacks of the angina revealed acute or subacute cardiac insufficiency, and the roentgen-ray a heart more distended than between attacks. After a course of ten to twelve intravenous injections of ouabain in $\frac{1}{4}$-mg. doses the diameters of the heart were diminished and clinical symptoms stopped. On the contrary when digitalis alone was used the original attacks were more numerous and more severe and the roentgen-ray showed a more marked distention of the left ventricle. Ouabain augments the systolic contraction of the ventricle by increasing the tone of the ventricular muscle, and the attacks of angina cease. Digitalis on the other hand slows the heart-rate by prolonging diastole, and an overdistention of an already distended ventricle results and precipitates an attack of angina and cardiac insufficiency. In conclusion the authors state that in cases of cardiac insufficiency with overdistention of the left ventricle digitalis may be poorly tolerated. When the heart-rate is regular and slow it may be harmful and in these cases ouabain is the medication of choice. In addition to the cases mentioned there may be borderline cases with decompensation and an acceleration and irregularity of rate. Digitalis then is useful, but should be preceded by a course of ouabain so that the permanent distention of the heart in systole may be decreased, and the heart muscle prepared for digitalization.

Constipation of Civilization and its Treatment with Substances which Increase the Bulk of Feces, Particularly Normacol.—Constipation of the present day, which is a result of the machine-age with a diet of meat,

fat and milk products which satisfy the protein requirements, but yield little residue, can be corrected according to the opinion of SCHINDLER (*München. med. Wchnschr.*, 1924, **33**, 1130) in two ways: (1) By substituting sport for the lack of muscular work and thus necessitating a diet higher in calories and of greater cellulose content, or (2) by adding substances to the diet which do not irritate the intestinal mucosa as do cathartics of various kinds and yet will regulate its activity. Linseed and psyllium seed are satisfactory and easy to take, but normacol made by the firm of Kahlbaum acts in the same way, but because of its greater affinity for water is much more effective. Normacol was used in 200 cases and in two forms. One form contained a trace of the extract of frangula, the other form was without it, and was called special normacol. Two teaspoonsful of the special normacol once or twice a day is the average dose. In the first weeks of treatment of this form of constipation and in cases of constipation due to proctitis or hemorrhoids the original normacol with frangula may be necessary.

The Precipitation of the Crisis in the Treatment of Pneumonia.—GARDNER MEDWIN (*Brit. Med. Jour.*, 1924, **2**, 49) reports the successful treatment of pneumonia by the precipitation of crisis by means of the subcutaneous or intramuscular injection of sodium nucleinate. From extensive experience during the pandemic of influenza in 1918 and 1919 in Alexandria it was discovered that injections of sodium nucleinate would cause a marked increase in the number of white cells whether the patient had a leukopenia or not, and simultaneously there was a corresponding improvement in the patient's condition. Records of 53 cases are reported and all except 8 responded to this treatment. In addition to the injections of sodium nucleinate sodium bicarbonate was given by mouth to the cases which showed signs of acidosis. In all cases of lobar pneumonia treated with sodium nucleinate there was rapid improvement, and in every case the crisis occurred within forty-eight to sixty hours after the first injection, no matter on what day of the disease it was administered. The preparation used for intramuscular injection was a solution of sodium nucleinate put up by the Clinical Laboratories of Paris in ampules of 2 cc containing 0.05 gm. to the cubic centimeter.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,
OF PHILADELPHIA.

Mental Health Problems in School Children.—EBAUGH (*Am. Jour. Dis. Child.*, 1924, **28**, 265) indicates the absolute necessity of close coöperation between the school authorities and mental clinics. Early maladjustment always is discoverable in school, and prompt study should be productive of results, and a great aid to the individual teacher

and school. The goal of education is to produce well-balanced persons who will adjust to their environment by meeting the realities of life instead of evading personal problems, and so developing faulty habits and poor social adaptation. Character training is as important as school instruction for efficiency and health. The cases summarized in his paper show the relation of emotional life, home environment, and training to school progress, and indicate the necessity for the study of the individual child in his total reactions to the school situation. The study of such a group of children is of practical significance when we consider that the school constitutes the real health center for the child of any district and affords the best chance for routine physical and mental examination. General ignorance of the principles of correct training of the child during the preschool and school age constitutes one of the most important public-health problems. To meet this problem, a closer relationship should be established between the school and the home through the agency of the visiting teacher, specially trained nurse and the social-service worker. Definite instruction in mental hygiene in all normal schools would be of great help to the teachers in lessening the routine problems that they meet in the management of behavior disorders in their pupils. School physicians trained in mental hygiene, school neuropsychiatric clinics in association with medical clinics and observation wards will be needed in this step. The basis of this paper is a study of 50 unselected cases referred by teachers of regular schools, and these have been summarized from the viewpoint of physical, mental, psychometric and environmental findings. Corrective modifications were suggested and the therapeutic results after a period of at least one year were recorded. The school was shown to be the ideal place for the study and correction of the maladjustments. The treatment cannot be undertaken too early in life.

The Intravenous Use of Mercurochrome-220 Soluble in the Treatment of Pneumonia in Children.—FREEMAN and HOPPE (*Am. Jour. Dis. Child.*, 1924, **28**, 310) found the intravenous use of mercurochrome of value in the treatment of pneumonias of infants and children. The results obtained by this drug were often spectacular. The course of the disease is sometimes shortened and often abruptly terminated. They report 12 cases of pneumonia occurring in infants and children who were treated by the intravenous use of mercurochrome-220 soluble. They also report the results of animal experimentation, showing that following the injection of mercurochrome the fluid squeezed from the lungs inhibits the growth of bacteria. Of the 12 cases of pneumonia 7 were bronchopneumonia and 5 were lobar pneumonia. Two patients died. In 1, death was inevitable before the drug was given. The other case, with cyanosis of unknown origin existing for several years, showed definite improvement at first, but later failed to respond to treatment. In 7 cases one injection was all that was required. Three cases required two injections and three injections were given in 2 cases. The average dose was 0.005 gm. per kilogram of body weight, using a 1 per cent solution. The authors call attention to the fact that a very marked clinical improvement usually occurs a few hours after the injection, and that this improvement sometimes occurs without any very marked change in the temperature or pulse-rate. They also observed

that these cases of pneumonia treated with mercurochrome ran a much shorter course than cases of pneumonia of the same severity when this drug was not used. The systemic reaction in children is mild.

The Effect of the Routine Administration of Cod-liver Oil on the Development of Rickets in the Breast-fed.—De Buys and von Meysenbug (*Am. Jour. Dis. Child.*, 1924, **28**, 329) based their studies on cranial bosses, costal beading, epiphyseal enlargement, flaring ribs and craniotabes. The cranial bosses was the most frequent symptom recorded. Costal beading, epiphyseal enlargement, flaring ribs, and craniotabes followed in the order named. These symptoms developed in spite of the use of an emulsion of pure Norwegian cod-liver oil in doses of one-half teaspoonful three times a day. The average intensity of each of these clinical symptoms was greater than in a former study where no cod-liver oil was administered, with the exception of epiphyseal enlargement and costal beading. In these two the average intensity was less in this study. All the symptoms began earlier in this study than in the previous one. During the first three months of the study there were eighty-nine hours less of actual sunshine and an average of 8.3 per cent less possible sunshine per month than in the same period in the previous study. The meteorological summary for the period of this study showed the percentage of possible sunshine to be 2 degrees above the normal average. It was 1.9 degree less than for the period of the previous study. The precipitation for the period of this study was 6.28 inches above the normal and 10.91 inches more than the precipitation for the period of the previous study. The atmospheric pressure temperature and humidity were about the same as for the previous study. The seasonal peak for the combined symptoms was noted in the month of July, the greatest height being July 26. The seasonal peak for this study differed from the peak of the previous study which occurred in the month of March. During the months of July and August the percentage of possible sunshine was at its minimum for the period of this study. The precipitation during this month was more than that for any two consecutive months in the study. The increase in the precipitation for July, 1923, over July, 1922, was greater than the increase of precipitation for March, 1922, over March, 1923. The total hours of actual sunshine for the period of this study was 116.8 less than for the period of the previous study. Considering rickets from the standpoint of clinical symptoms, the disease was beneficially affected by the routine use of cod-liver oil in spite of the adverse meteorological conditions. Considered from the standpoint of all clinical symptoms sunshine and precipitation seemed to have an influence on the severity of rickets even in the presence of the administration of cod-liver oil.

Clinical Studies of Some Diseases of the Blood in Children with Illustrative Cases.—Griffith (*Arch. Pediat.*, 1924, **41**, 511) reports a number of cases and he feels that the blood-picture in chlorosis is of very frequent occurrence in infancy and childhood, and that such cases should be properly designated as chlorosis. The administration of iron, without any other treatment, is often of striking benefit in these cases and in simple anemia. In diseases of the blood in general, especially in childhood, the symptoms appear to be to a certain extent inter-

changeable. Without an examination of the blood a diagnosis is more likely to be mistaken than correct, and even with it a certain diagnosis cannot be based upon any one hematological feature. This is especially true of alteration in the character of the red cells, any excess either of lymphocytes or myelocytes, a high-color index or a low-color index. There appears to exist no definite relationship between the degree of alteration of the blood and that of the size of the lymphatic glands and the spleen. Variations in the blood-picture occur not only between different cases, making the differentiation of the disease present difficult, but from time to time impossible in the same case. Only careful and often repeated examinations of the blood and of the symptoms in general insure the arrival at the correct diagnosis.

A Clinical Study of Lactic Acid Milk as a Routine Feeding for Sick and Healthy Infants.—FIELD (*Arch. Pediat.*, 1924, **41**, 541) claims that lactic acid milk is better for artificially fed infants than sweet milk because the protein in acid milk is precipitated as a fine flocculent curd and remains so in the stomach until the process of digestion has broken it down. The boiling of raw milk partially accomplishes the same thing but also partially destroys the vitamines. An extremely important factor in selecting a food for young infants is its "buffer" or acid binding qualities. Lactic acid milk is similar in this respect to breast milk, the pH of the gastric contents at the height of digestion of a group of infants fed on whole lactic acid milk having been found to be 3.71, while the average hydrogen-ion concentration of the stomach contents of the same group fed on breast milk was 3.75, which is probably about the optimum concentration for gastric digestion in infants under one year. In sick infants it has been shown that the actual concentration of hydrogen ions in the gastric contents averaged only one-tenth as much as that for normal infants receiving the same food, which was breast milk. It seems, therefore, rational to avoid sweet milk in feeding sick infants for thereby we diminish gastric acidity. The acid of the gastric contents when present in sufficient amounts permits peptic digestion of proteids, influences gastric mobility, and has a very definite antiseptic action. The acidity of the gastric contents is known to regulate in some measure the pyloric reflex, and acid in the gastrointestinal tract stimulates the flow of pancreatic juice, bile and intestinal secretions, and results in distinctly better absorption of all the food elements. A third reason why lactic acid milk is better than sweet milk for feeding infants is that it is practically sterile even under the most adverse conditions, or rather under the most favorable conditions for bacterial growth. In lactic acid milk there is a maximum of food value with a minimum of bulk, which in many cases is of distinct value.

Medical Aspects of Acute Appendicitis in Children.—HOWLAND (*Jour. Am. Med. Assn.*, 1924, **83**, 961) says that there is justification for dreading this disease in the very young because the attacks are usually severe. Mild attacks, comparable to those encountered in later life, are distinctly rare. General peritonitis may intervene as early as the second or third day. It is not proper to conclude that this is the rule. Many patients have lived as long as would an adult, and the process has remained localized for days and sometimes even for weeks.

Howland agrees with Drachter that the problem of appendicitis in the young child is one of diagnosis, and that if operation is performed before there is a general peritonitis or pocketing of pus in numerous places, the mortality of appendicitis should be no greater but should be even less than it is with the adult.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

JOHN H. STOKES, M.D.,

PROFESSOR OF DERMATOLOGY AND SYPHILOLOGY AT THE SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA.

The Treatment of Syphilis from an Experimental Point of View.—This article by BROWN and PEARCE (*Ann. Clin. Med.*, 1924, **3**, 1), a summary from the experience of two of the most profound students of experimental syphilis, should be read in full by all who are called upon to deal with the difficult and perplexing issues of modern syphilotherapeutics. It is only possible in an abstract to single out a few specially effective statements from a text which maintains a rare plane of insight and breadth of knowledge of the problems of the disease. The authors, reviewing the past decade in the treatment of syphilis, conclude that it cannot be said that any considerable progress has been made in the treatment of syphilis in the last few years. The noteworthy improvements have been mainly in the technic of application of known remedies. Experience has shown that it is not sufficient to regard syphilis merely as a spirochetal infection to be attacked by the use of the most vigorous parasiticidal measures that the patient will endure. The treatment of syphilis is something more than this. It is in a sense a combination of applied pathology and pharmacology, in that the selection and use of any therapeutic measure must be determined by the fitness of such a measure to meet the needs of a given situation. Not only must one know syphilis in all its manifestations, but there is also need for an intimate knowledge of the human economy; for after all we do not treat the spirochete or even the disease, but we treat the patient, and the resources of the patient are destined to become more and more important. Among many orienting facts which must be kept in mind, we should remember that syphilis begins insidiously and that the invading organism is widely distributed before any clinical manifestations of the disease appear. The action of therapeutic agents has been and is but imperfectly understood. Innumerable estimations of trypanocidal and spirocheticidal action and of toxicity have been made, together with exhaustive studies of absorbtion, elimination and distribution. But nowhere is there to be found a comprehensive report of the biologic action of even such substances as arsphenamin and neoarsphenamin. During the early stages of acquired syphilis our efforts may be concentrated on the destruction of parasites, but once a characteristic lesion has developed it is useless to try to prevent a systemic distribution

of the organisms. It is, however, still possible to prevent the localization and growth of spirochetes in inaccessible foci and to prevent the development of lesions which afford more or less protection against the actions of spirochetal agents (that is, fibrosis and endarteritis obliterans). In very early cases the spirillicidal action of the drugs is therefore most important. The effect procedes almost like a test-tube reaction. Yet even in the earliest cases some of the spirochetes may be inaccessible. Hence other things being equal, penetrating power as well as mere spirillicidal action must be considered among the qualities required of the drug used. The ability of the selected drug to cause resolution of lesions (healing) with resultant exposure of the organisms to its effects, must also be considered. Wide differences exist between the interrelations of these qualities in different drugs now in use. Some are parasiticidal in the blood stream but ineffective in tissue because they cannot penetrate it. Others, weakly spirillicidal, are more effective in spite of this deficiency, because of their increased penetrating power. In the advanced stages of syphilis, the hope of effecting a complete sterilization is greatly diminished by the changes that have occurred in the host. The penetrating power of the agents used therefore becomes the more important as the foci become more difficult of access. in dealing with the general immunologic problems of the disease, it should be remembered that all therapeutic agents that cause an abrupt cessation of the reaction on the part of the patient to his disease, as indicated by a rapid resolution of lesions, but which fail to destroy all the infecting organisms, operate to the disadvantage of the patient and predispose to the subsequent occurrence of more severe manifestations. In part this effect is attributable merely to the removal of the stimulus to reaction resulting from actual destruction or temporary suspension of the activity of the spirochetes. In other instances however, there is definite and more or less persistent reduction of the effectiveness of the reaction due to the effect of the drug on the patient. Moreover in cases of this kind, the earlier the treatment is undertaken the more serious are the consequences of failure on account of interference with immunologic reactions. It appears from the observations of Chesney and Kemp that permitting the immunologic reactions to develop to their full force leaves the animal after subsequent sterilizing treatment, immune or at least refractory to reinfection, although no remnant of the old infection can be demonstrated to explain the immunity. Moreover, there are remarkable differences in the character of the disease which can be produced by the use of a given procedure at different seasons of the year or in different years. It has been shown, too (Pearce) that iodids, known to be without spirillicidal effect, are able when used alone, to modify in a favorable manner, the course of experimental syphilis. Facts such as these indicate very clearly that the ability to combat a syphilitic infection is an inherent constitutional trait. It is not, however, a fixed property, but may increase or diminish with age, with season, climate and meteorologic conditions, and with changes in the physical condition of the animal. The condition of the endocrine mechanism and changes in this group of structures and in the lymphatic system are especially instrumental in determining the course of an infection. It has been found that the removal of a part or

the whole of such an organ as the thyroid will produce a profound alteration in the character and efficiency of the response of such animals to syphilitic infection. The mass relations of various organs of the body at various seasons and under varying conditions of sunlight can be correlated with change in the resistance of these same animals to syphilitic infection.

Treatment Results in Early Syphilis.—MUTSCHLER (*Arch. f. Dermat. u. Syph.*, 1924, **147**, 105) reports the results of three years' observation of 55 cases of primary syphilis, 21 of them Wassermann negative on the blood and of from three to four weeks duration, and 31 with positive blood Wassermann reactions and a duration of four to ten weeks. The treatment used consisted of 10 to 12 injections per course of arsphenamin or silver arsphenamin, alternating or combined with calomel, novasurol or gray oil. Two such courses were given in the more advanced cases one course only in many of the earlier cases. The results were checked by spinal fluid and blood Wassermann examinations, physical examination with emphasis on lymphadenitis, etc. It is estimated that in the seronegative group, 100 per cent of cures have been obtained. In the seropositive group, the relapses aggregate 50 per cent in those treated with only one course, and no relapses in those receiving two courses. It should be noted that the individual courses are considerably more intensive than those customary in this country. Mutschler cited Silberstein who reported from Schlotz's Clinic 80 per cent of cures in a long period of observation of the very early cases, this result being obtained with one intensive course.

The Problem of Arsphenamin Resistant Syphilis.—SILBERSTEIN (*Arch. f. Dermat. u. Syph.*, 1924, **147**, 116) discusses on the basis of the experience of Scholtz's Clinic, covering a period from 1911 to the present time, whether or not there is developing an arsphenamin resistant syphilis. Silberstein cites the experience and impressions of a number of observers in support of the belief that there is developing a distinctly arsphenamin resistant type even of early syphilis, which requires longer and more frequently repeated courses, which in spite of their increasing intensity fail to produce the results obtainable with the drug in the first years of the past decade. He directs attention also to the growing volume of reports on arsphenamin resistant syphilis in the literature. He constructs from the experience of the Scholtz Clinic a very interesting table, evidencing the increasing resistance of early syphilis to methods of treatment which were effective in the earlier days, as follows: The Wassermann reaction became negative in the years 1911–1916: In 236 patients after one series of treatments, 198 times or 85 per cent; in the remaining 38 patients after 2 series, 30 times or 78 per cent.; in the remaining 8 patients after 3 to 4 series, 8 times or 33 per cent. The Wassermann reaction became negative in the years 1921–1922: In 60 patients after 1 series, 14 times or 23 per cent; in the remaining 46 patients after 2 series, 25 times or 54 per cent; in the remaining 21 patients after 3 to 4 series, 7 times or 33 per cent. It was rare, the author states, to observe an irreversible positive before the war, yet

since the war such cases aggregate 23 per cent of the total treated. After considering the various possibilities which may explain this very obvious difference in the treatability of the disease during the past decade, the author concludes that a difference in the resistance of current strains, so to speak, of Spirochæta pallida to arsenicals, actually exists, and that the necessity for massive early treatment and varied methods becomes therefore the more urgent as time elapses. Ehrlich, in one of his discussion of chemotherapeutic problems as applied to syphilis, indeed foreshadowed this very possibility.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Cesarean Section for Occlusion of the Vagina and Calculus.—Fretz (*Brit. Med. Jour.*, August 23, 1924) reports the case of an East Indian woman who had been in unsuccessful labor and was brought to a hospital. On examination there was absolute occlusion of the upper two-thirds of the vagina by a dense fibrous band. The cervix could not be found. On the anterior vaginal wall in front of the adhesion was a hard calcareous mass which, on removal, proved to be a phosphatic stone. After its removal urine trickled into the vagina, showing the presence of a fistula. It is thought that the fibrous obstruction was caused by the chronic irritation from the fistula. The patient was successfully delivered by Cesarean section and did well until the twelfth day. She then became maniacal and died of exhaustion on the sixteenth day. The child survived.

The Sheppard-Towner Act.—In the *Journal of the American Medical Association*, September 13, 1924, is published an editorial calling attention to the recent statement of work accomplished by the Government under this Act. In 1922, 43 states coöperated, 41 in 1923, 40 in 1924. Analyzing all claims made for the Act, there were four, of which the first three amount practically to nothing, as they state that the activities of states and local communities have been increased, and that the quality of work done for mothers and babies has improved. It did not require the Sheppard-Towner Act to accomplish this, for the profession had been working steadily for this purpose for a number of years with excellent results. The fourth claim for accomplishment is that state appropriations have increased with the passage of the Act. It must be remembered that under the Act states have been forced to appropriate money and that such appropriation does not represent a voluntary and enthusiastic accomplishment. If the advocates of this measure would justify the Bill, they must submit exact figures indicating that the maternal and infant death-rates have been appreciably lowered in those states which have coöperated with the Federal Government, and that the rates of expenditure are much lower than those obtaining

before this meddlesome legislation became effective, and that such rates are lower than those in states which have not coöperated. The defendants of the Act cannot ignore the tendency to increased activity and improvement in results which had been begun before the passage of the Act.

The Relation of Venereal Disease to Childbirth.—SCHUMANN (*Am. Jour. Obst.*, September, 1924) has examined 150 private cases by taking a smear from the cervix, with one positive result, and that a doubtful one not confirmed by subsequent examination. He believes that gonorrhea is much less common in pregnant women than is often stated. In cases of sterility this infection is a most important element and should such a patient conceive, abortion and pelvic inflammation frequently follow. He draws attention to the studies of Curtis showing that the tube is not the focus for chronic gonorrheal infection in the majority of cases. Gonorrhea is a widespread and pernicious agent in producing tubal pregnancy. Where this disease complicates pregnancy, vigorous manipulations should be avoided, the entire vagina and cervix should be gently coated once each week with 20 per cent argyrol solution and the patient should be instructed to fill the vagina with 10 per cent argyrol solution daily, using from 2 to 4 ounces, given by a soft rubber bulb syringe and held in place twenty minutes by closing the labia with the fingers. Chronic endocervicitis requires treatment when it produces a profuse irritating discharge, equal parts of sodium bicarbonate and Fuller's earth, placed in the vagina and retained forty-eight hours by cotton tampon, will improve the condition. At labor the birth canal should be flushed with 10 per cent argyrol solution. The solution should be allowed to remain until expelled by labor contractions. It is of great importance that the patient be not wounded by applications, and early interference in labor is to be avoided. General septic infection may be readily induced by unskilful manipulations. He calls attention to granuloma inguinale as not infrequent and occasionally complicating pregnancy. The fact that the external genital organs become the site of highly proliferous masses with foul discharge, makes vaginal delivery impossible. The treatment of the condition during pregnancy is unsuccessful and delivery by Cesarean section so soon as the child is viable, is indicated. In studying the effect produced by syphilis upon parturition, 48.4 per cent of syphilitic women gave birth to living and healthy children who gave no evidence of infection. The writer's study of the subject leads him to believe that syphilitic pregnant women, without treatment, will give birth to living and healthy children showing no evidence of syphilis in about one-half of the cases; about one-third produce syphilitic children either living or dead, 10 per cent of the whole number observed. In the remaining cases it is impossible to clearly recognize the presence or absence of syphilis. This and similar observations would lead to the belief that syphilis is not increasing throughout the world. Colles' law is still recognized and parental infection of the ovum is acknowledged. Profita's law which holds that syphilitic women may give birth to a child that is free from this disease and that never presents any manifestations of it, is also true. The general belief of the writer's study is that the steady increase of prenatal care and early recognition of disease in pregnant patients, with active and persistent treatment, is improving this condition very materially.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

INSTRUCTOR IN GYNECOLOGY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Significance of Hematuria.—In a brief clinical study of 821 consecutive cases of hematuria, in all of which blood was grossly visible, MacKenzie (*Surg., Gynec. and Obst.*, 1924, **39**, 155) reminds us that the presence of macroscopical blood in the urine can be due to a great variety of causes, and generally signifies some serious pathological condition of the urinary tract. It is not a clinical entity which requires treatment but a symptom which demands investigation. The importance of hematuria and the necessity of determining its cause must be recognized by every physician and should be carefully impressed upon each patient suffering from urinary hemorrhage. Notwithstanding all that has been said and written on this subject, there is still a tendency for the medical profession to regard this condition lightly, to treat it without a diagnosis, and to consider a cessation of bleeding as an indication of cure. This is largely due to the fact that hematuria is usually intermittent in character. During the free interval, while the patient is apparently in perfect health, it is not surprising that both patient and physician should minimize the importance of this danger signal. It is at this time, while there is yet a probability of cure, that the best opportunity for investigation and diagnosis is afforded. An analysis of the 821 cases in this series shows that in 192 cases the hemorrhage was due to calculi, 113 to tumors, 88 to renal tuberculosis, and 143 to surgical infections of the ureters and kidneys; or, excluding the urethra, 536 cases out of 761, that is more than 70 per cent were caused by calculi, tuberculosis, cancer or surgical lesions of the kidney; while the other 30 per cent most certainly required investigation. The great importance of subjecting these patients to a careful and thorough examination is at once apparent. With the present day methods of diagnosis the origin and cause of urinary hemorrhage can be ascertained in a very large percentage of cases.

Operative Results in Cervical Cancer.—The Hunterian Lecture delivered by Forsdike (*Brit. Med. Jour.*, 1924, **2**, 94) before the Royal College of Surgeons in 1924 was devoted to the important subject of cancer of the uterine cervix. He reminded his audience that the operative treatment of cancer of the cervix had undergone great changes in the last twenty-five years—local excision of the disease by knife or cautery, supravaginal amputation of the cervix, vaginal hysterectomy, and last of all, the radical abdominal operation. The limits of this last

operation vary with the individual surgeon, from panhysterectomy with excision of as much parametrial and vaginal tissue as possible, to resection of bladder, ureters, bowel and more or less of the pelvic fascia glands. The mortality in the more extensive operations is as high as 70 per cent and probably is rarely below 30 per cent, the average for all cases is 20 per cent and for early cases 6 per cent. The radical operation has been widely practised for twenty years and for early cases it has general support, but there is an increasing number of surgeons who question the wisdom of applying this operation to cancer which has clinically extended into the pericervical tissues, for the results are deplorable and of those who survive the operation less than 10 per cent are alive a year later. All surgeons admit that the results warrant operation in the early cases, while in the advanced cases no surgery should be done, but it is the borderline group where opinions differ markedly. Forsdike has records of 50 borderline cases treated by the radical operation in which the parametria were infiltrated by the growth, many of which came under his observation for treatment of the recurrence of the growth. The most striking feature of this series is the large number of early recurrences and the consequent relief was so transient as to be negligible. Of the 50 cases, 10 are living and 40 are dead. Of the 10 alive, 6 remain well over periods of five and a half, four and a half, four, four, three and a half, and three years, 2 remain well between one and two years, 2 are alive with recurrence under twelve months. Thus the high mortality, rapid recurrence and poor end-results cast grave doubt upon the wisdom of radical operation in this group since there are ample reports from various countries which show that the results from radium far surpass those from operation in such cases.

Treatment of Uterine Fibroids.—In his discourse upon the treatment of the various types of uterine fibroids CUTHBERT LOCKYER (*Brit. Med. Jour.*, 1924, **1**, 1037) of London, who is certainly well qualified to speak states that he regards deep myomectomy, which is being revived, as involving somewhat greater risk than a supravaginal amputation, but this additional risk should be ignored if there is a chance of subsequent childbearing. When hysterectomy is indicated there is always a discussion as to whether the operation should be a total or subtotal hysterectomy and there are many good men supporting each side of the question. Lockyer is very broad-minded in his observations and believes that there are indications for both types of operation although if he had to confine himself to one or the other he would become a "totalist." It is not difficult to understand his choice because he has performed 195 total hysterectomies with 3 deaths, a mortality of 1.54 per cent, while in his series of supravaginal amputations numbering 284 cases there were 5 deaths, a mortality of 1.76 per cent. It is extremely doubtful however whether the great majority of surgeons could keep their mortality as low as this in either type of operation, especially the total operation. As regards morbidity, he states that simple cases run as smoothly after the total as after the subtotal operation and purulent cases do better with the vaginal drainage afforded by the total operation than without, but nevertheless these considerations do not justify the abolition of the subtotal operation since it is easier and quicker and may

be justifiable where the longer, more tedious and bloody procedure would not. In regard to the question of ovarian conservation, Lockyer believes that it is better to conserve one or both ovaries, if healthy, no matter what the age of the patient may be, thus he is opposed to the frequently heard statement that it is better to remove the ovaries if the patient is beyond forty years of age. In conclusion he states that in 55 per cent of all fibroids, no treatment whatever is needed. In the remaining 45 per cent, 35 per cent require removal by some type of surgical operation, leaving 10 per cent to be dealt with by radium. This is equivalent to stating that the field of operation is from three to four times as great as that for radiotherapy.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
OSKAR KLOTZ, M.D., C.M.,
PROFESSOR OF PATHOLOGY, UNIVERSITY OF TORONTO; TORONTO, CANADA.
AND
DE WAYNE G. RICHEY, B.S., M.D.,
ASSISTANT PROFESSOR OF PATHOLOGY, UNIVERSITY OF PITTSBURGH; PITTSBURGH, PA.

Properties of Purified Dick Scarlatinal Toxin.—"The Dick scarlatinal toxin is the filtrate from the growth in broth of certain streptococci isolated from the throats of scarlet fever cases, as has been shown by the Dicks, Dochez and Sherman." The toxic substance is produced in the largest quantities after the addition of considerable amounts of horse blood. HUNTOON (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 513) found, after numerous investigations, that the best toxin was produced by seven-day growths; that the toxic substance is not of the nature of a globulin, but is precipitated with the higher albumin factions; that it is a protein which is destroyed or inactivated by trypsin, and by heat (90° for one hour); that its tendency to come down in a narrow range of ammonium sulphate precipitation renders a high degree of purification possible; and that the material is neutralized by convalescent serum, but is not neutralized by normal horse serum or by the serum of horses immunized against the scarlet fever streptococcus in the ordinary manner (non-toxic substances).

Kidney Changes in Pyloric Obstruction.—ZEMAN, FRIEDMAN and MANN (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 179) discovered, in the routine microscopical examination of autopsy material, almost identical kidney changes in 4 cases of pyloric obstruction. Two of the 4 cases exhibited, clinically, typical tetany. The renal changes consisted in degeneration of cells lining the spiral and terminal straight portions of the first convoluted tubules. In many sections these cells were necrotic and infiltrated by granules staining dark blue with hematoxylin, which merged into larger masses, entirely blocking lumina of tubules. The authors interpreted the blue staining granules as calcium

salts. The renal changes described in these cases were very similar to those noted in mercuric chlorid poisoning. The authors cannot consider these changes as evidences of nephritis, inasmuch as they were entirely degenerative in nature, being best designated by the term toxic degenerative nephrosis. Similar cases have been reported, recently, by Brown, Hartman, Eusterman and Rowntree, who attributed the presence of calcium in the kidneys to the fact that the patients had received calcium by mouth. The authors cannot subscribe to this view, believing that the primary factor is pyloric or high duodenal obstruction in association with repeated vomiting, to which the tetany and kidney changes appear to be secondary. They are unable to explain satisfactorily at present the mechanism leading to the kidney damage. Sections of the stomach and other organs in their series showed no deposit of calcium such as occurs in metastatic calcification where the amount of circulating calcium is increased.

Certain Pathological Tissue Changes in Thyroidectomized Sheep.—Of 10 lambs that were thyroidectomized early in life by GOLDBERG and SIMPSON (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 567), 5 showed marked lesions. These consisted of subcutaneous and subserous edema with, in most cases, ascites and hydrothorax. The kidneys showed parenchymatous nephritis. The most striking changes occurred in the aorta and pulmonary arteries, which exhibited hyaline degeneration and calcification of the media in the form of plaques. There was a striking absence of fatty degeneration in any of the vessels. The controls did not show any of these tissue changes. The observations extended over a period varying from eight months to two and a half years after the removal of the thyroids. The authors believe that the arteriosclerosis can be explained on a chemical basis, perhaps due to senile changes occurring early in life as a result of complete thyroidectomy.

The Effect of Digestive Juices on the Potency of Botulinus Toxin.—"It is a general rule that the true toxins derived from culture of pathogenic microörganisms must be introduced parenterally if they are to act on the animal organism. When given by mouth, even in very large amounts, they tend to be harmless. The failure of the toxins to act under these circumstances is ordinarily ascribed to the fact that they are subject to destruction by the digestive juices. *Botulinus* toxin, however, presents a notable exception to the rule just mentioned." After a number of experiments on mice, BRONFENBRENNER and SCHLESINGER (*Jour. Exper. Med.*, 1924, **39**, 509) found that *botulinus* toxin resists a degree of acidity equivalent to that of the stomach even when exposed thereto for twenty-four hours at 37° C. The toxin was less resistant to alkali, however, as shown by the fact that in a medium of weakly alkaline reaction its potency was reduced to less than one-tenth in twenty-four hours. It was unaffected by peptic or tryptic digestion. "Because of its instability in mildly alkaline solutions and resistance to acid, there is reason to believe that the toxin is in the main absorbed from the upper portion of the digestive tract; that is to say, from the stomach and upper duodenum."

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Life Tables for the Population of New York State According to Nativity.—DEPORTE (*Am. Jour. Hyg.*, 1924, **4**, 302) studied life tables for white males, aged twenty years and over, of the population of the state of New York with reference to native-born of native parentage, native-born of foreign or mixed parentage and foreign-born, based on the average number of deaths in the years 1909, 1910, 1911, as given in the U. S. Mortality Reports, and the population, as given in the U. S Census Report, 1910. He states in one of his several conclusions that conditions are more favorable among foreign-born than among native-born of foreign and mixed parentage. This, he believes, is due partly to natural selection, artificial selections and occupational differences, but mainly to the unwise social pressure toward superficial Americanization, as a result of which a large fraction of the native-born of foreign parentage become strangers to their parents, grow up without home influences, forsaking the culture and traditions of their people, and finding nothing in the life of the street to take their place. The reason cannot be the biological weakness of a blend, since the native-born of the first generation are in most cases products of the same racial strain. This opinion finds support in the fact that in Minnesota, where the population is still largely rural, where the foreign-born and the native-born have been from the beginning of settlement of the same Teutonic stock—English, German, Scandinavian, where the neighbors of a native-born person were very likely people of the same or similar strain, and of comparatively recent origin, where the old-home traditions of the peoples had not been held in contempt, and where therefore Americanization was a process of addition and not of total rejection of everything "foreign"—in Minnesota, in 1910 and 1920, the relation between the death-rates of native-born of the first generation and of foreign-born had been the reverse of what we found it to be in New York.

Occurrence of Leptospira Icterohemorrhagiæ in Wild Rats of Baltimore.—ROBINSON (*Am. Jour. Hyg.*, 1924, **4**, 327) noted that the animals bearing traumatic scars were most likely to be infected. Therefore, he states it is possible that wild rats are normally infected through abrasions of the skin. While the number of examinations made is not large enough to establish generalities, yet the results tend to show that about 7 per cent of the wild rats of Baltimore are infected with Lepto-

spira icterohemorrhagiæ. Dark-field examination of kidney emulsions gives a larger percentage of positive findings than guinea-pig inoculation. Certain strains are without virulence for guinea-pigs. The carrier condition can be produced in white rats, and the leptospiras retain their virulence undiminished after at least four months in the white rat. Carriers are most likely to be large full-grown animals.

The Biseasonal Prevalence of Infantile Paralysis (Acute Anterior Poliomyelitis).—Aycock and Eaton (*Am. Jour. Hyg.*, 1924, **4**, 364) studied the seasonal prevalence of infantile paralysis in the United States over a period of eleven years (1912–1922). They found a marked regularity in the summer prevalence of the disease. A definite secondary increase in its occurrence, usually in March or April, has been established. The authors state that this increase occurs with fair regularity from year to year, and with a certain degree of uniformity in all parts of the country. This suggests the possibility of two modes of transmission of infantile paralysis.

The Relations between a Carnivorous Diet and Mammalian Infections with Intestinal Protozoa.—Hegner (*Am. Jour. Hyg.*, 1924, **4**, 393) states that three rats that were fed throughout their lives (one hundred and seventy-four days) on a carnivorous diet were found to be free from Giardia muris and Trichomonas muris. Two of these rats contained a few specimens of Hexamitus muris. A review of the literature of protozoölogy reveals the fact that intestinal protozoa (amœbæ ciliates and flagellates) have not been reported from carnivorous mammals in nature except very rarely. Examinations were made of fecal specimens, at intervals during a period of seventeen days, from twelve carnivorous animals belonging to ten species (lion, tiger, polar bear, grizzly bear, black bear, Syrian bear, gray wolf, gray fox, red fox, wild cat). No protozoa of any kind were discovered except Giardia cysts in the wild cat. Data from the various sources seem to prove that a carnivorous diet is unfavorable for the intestinal protozoa of mammals.

The Protection of Dogs against Rabies by Umeno's Method of Preventive Inoculation.—Hata (*Jour. Immunol.*, 1924, **9**, 89) presents the results of 104,629 preventive inoculations of dogs against rabies in Tokio and Yokohama and their environs during the period since the adoption of Umeno's prophylactic method. Only 41 of the inoculated dogs developed rabies, while 1699 of the uninoculated group contracted the disease, notwithstanding the latter group represented only one-third of the total number of dogs in the two prefectures.

Notice to Contributors.—All communications intended for insertion in the Original Department of this Journal are received only *with the distinct understanding that they are contributed exclusively to this* Journal.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this Journal, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

Dr. John H. Musser, Jr., 262 S. 21st Street, Philadelphia, Pa., U. S. A.

INDEX.

A

Abscess, pulmonary, etiology and treatment of, 446, 447
Actinomycosis, 607
Alexander, J., surgery of pulmonary tuberculosis, 1, 268, 412, 574
Alkali in dye therapy, 98
Allergic phenomena, 611
Appendectomies at the Lankenau Hospital, 608
Appendicitis, chronic, 807
  in children, 295, 302, 918
  two hundred and sixty-two consecutive cases of, 608
Anemia, Addison's, 137
  splenic, 836
Aneurysm, mycotic, gonococcal and pneumococcal in origin, 381
  of the thoracic aorta, 654
Angina pectoris, 786
Ankle-joint, fractures of, 607
Anopheles, observations on, 156
Antidote for arsenic, bismuth and mercury poisoning, 764
Antimony compounds for intravenous use, 728
Antiseptic, efficient intestinal, 450
Arsphenamin death, 142
  resistant syphilis, 921
  solutions, viscosity and toxicity of, 311
Arterial occlusion, coronary, 181
Arthritis deformans, sulphur in treatment of, 77
Aschner, P. W., experimental biliary drainage in the dog, 749
  pressure factors in the biliary-duct system of the dog, 812
Asthma, treatment of, 297, 448
Atropin, some cardiac effects of, 641
Auricular flutter, 893

B

Bacillus hystolyticus, recovery of, from human feces, 309
  sporogenes, serological agglutination of, 153
Bacteria in the lungs of alcoholized mice, 779
Bacteriological study of extirpated tonsils, 623
Bartlett, F. H., tuberculosis in infancy, 704
Bassler, A., observation of fat digestion for clinical study and physiological demonstration, 869
Begg A. C., insulin in general practice, 902
Bilharziasis, treatment of, by antimony tartrate, 763
Biliary drainage in the dog, 749
Bilirubinemia in patients treated with arsphenamin, 768
Bi-seasonal prevalence of infantile paralysis, 929
Blackford, L. M., comparison of blood-platelet count in splenic, arterial and venous blood, 723
Blood chemistry in pregnancy, 773
  composition and properties of, 511
  corpuscles in the newborn period, 300
  of irradiation, effect on, 215
  platelet count in splenic, arterial and venous blood, 723
  pressure, high, 138
  smears in the diagnosis of pertussis, 453
  transfusion, 298, 534
Boardman, W. W., phenoltetrachlorphthalein in the study of liver function, 688
Bone marrow and spleen in the treatment of anemia, 819
Botulinus toxin, digestive juices on the potency of, 927
  studies on, 463
Boyd, Linn J., aneurysm of the thoracic aorta, 654
Breast, tumors of the, 799
Brown, G. E., coronary sclerosis, 165
Bulmer, F. M. R., some cardiac effects of atropin, 641
Burke, V., value of alkali in dye therapy, 98

C

Cancer of the cervix, 618
  high voltage roentgen therapy of, 775

Carbuncle and its treatment by magnesium sulphate, 764
Carcinoma of the liver, primary, 241
Cardiopathies, nasal accessory sinuses in, 910
Carnivorous diet and mammalian infections with intestinal protozoa, 929
Catalytic action of copper in the destruction of antiscorbutic vitamin in milk, 778
Cervical cancer, operative results in, 924
Cesarean section for occlusion of the vagina and calculus, 922
Children, diseases of the blood in, 917
intestinal obstruction in, 766
Cholelithiasis, studies in, 66
Circulation, the renal, 134
Clark, W. E., splenic anemia, 836
Clarke, N. E., a comparative study in digifolin administration, 201
Clawson, B. J., myocardium in non-infectious myocardial failure, 648
Cod-liver oil in development of rickets in the breast-fed, 917
Constipation of civilization, 914
Contraception, 456
Coryza, human inoculations with filtered nasal secretions from, 467
Crile, G. W., endocrinology from the point of view of the surgeon, 625

D

Death, a new vascular sign of, 893
Deaths among taxpayers and non-taxpayers of income tax, Providence, 1865, 776
Dermatoses due to cosmetics, 767
Dermatosis, familial, 143
Diabetes mellitus, cause of death in, 313
surgery, 495
Diagnosis, difficult, during pregnancy, 455
Diaphragm, eventration of, 445
Dick test in normal individuals and in acute and convalescent cases of scarlet fever, 461
Digifolin administration, a comparative study in, 201
Digitalis in certain types of cardiac insufficiency, 914
therapeutic use of, 762
Diphtheria, effect of freezing on toxin-antitoxin mixtures, 301
myocardial lesions of, 624
Diseases of infancy and childhood, relation of heredity to, 299
Dislocation, congenital, 446
Dog, biliary-duct system of the, 812
Dogs, protection of, against rabies by Umeno's method of preventive inoculation, 929
Drainage of the perivesical region, 447
Drug addiction in the United States, 131
Duodenal drainage, rational use of, 761
Duodenum, stenosis of the, 913

E

Eck, C. P., use of tryparsamide in neurosyphilis, 157
Empyema, acute, 296
in children, mortality from, 912
Encephalitis in children, 765
Endocarditis, valvular and mural, 292
Endocrinology from the point of view of the surgeon, 625
Enteric infections, cutaneous hypersensitiveness in, 131
Epididymitis, epididymotomy for, 447
Epilepsy, idiopathic, 635
Erdmann, J. F., tumors of the breast, 799
Evans, J. S., bone-marrow and spleen in the treatment of anemia, 819
Exsanguination-transfusion, 909
Ex-service man and his lungs, 910

F

Face, malignant growths about the, 295
Fat digestion for clinical study and physiological demonstration, 869
Femoral hernial sac, etiology of the, 913
Fitz, R., cause of death in diabetes mellitus, 313
Flat foot, mechanism of the normal and of the, 134
Fleisher, M. S., relation of Fungi imperfecti to diarrheal conditions, 371
Foot-and-mouth disease, cause of, 777
Fracture of the anterior-superior spine of the ilium, 296
occurring in civil life, 294
Fried, B. M., primary carcinoma of the liver 241
Fried, H., primary cancer of the liver, 875
Friedenwald, J., primary cancer of the liver, 875
Fungi imperfecti, relation of to diarrheal conditions, 371

G

Gall-bladder, infection of, in relation to pernicious anemia, 469
pathology, 608
Gall stones in women, 446
Garvey, J. L., sclerosis of the spinal cord and carcinoma of the stomach, 847

Gastric ulcer, 137
Gastroenterostomy, unabsorbable sutures in, 913
Gibson, C. L., chronic appendicitis, 807
Gilliam operation, 620
Goiter, 445
  action of iodid in, 297
  effect of iodin in, 909
Gold-sol reaction, 618
Goldstein, I., the human dying heart, 388
Gonorrhea in the female, treatment of chronic, 776
  in women, 305
Gonorrheal complement-fixation test in women, 149
Gordinier, H. C., coronary arterial occlusion, 181
Grafts, testicular, 447
Gram, H. C., composition and physical properties of the normal human blood, 511
Gray, H., lipoids in 1000 diabetic bloods, 35
Grieve, I., value of alkali in dye therapy, 98
Guinea-pigs, tuberculous, 546

H

Hamman, L., angina pectoris, prognosis of, 786
Heart disease, 781
  deaths and disabilities from, 779
  disturbance of, produced by pregnancy, 457
Hematological responses to injections of streptococci, 115
Hematuria, significance of, 924
Hepatitis, 609
Herpes zoster in Hodgkin's disease, 326
  etiology of, 616
Hexamethylene dermatitis in the rubber industry, 768
Hinton, J. W., exophthalmic goiter, 629
Hodgkin's disease, herpes zoster in, 326
Holloway, J. K., comparison of blood-platelet count in splenic, arterial and venous blood, 723
Hookworm disease, control of, 311
  larvæ, notes on the longevity and infectivity of, 467
Horgan, E., splenic anemia, 836
Human dying heart, 388
  hypersensitiveness, 312
Hydrops gravidarum, 145
Hypertension, problems in, 668
Hysterectomy as operation of choice, 460

I

Infancy, wasting disorders of, 301
Influenza, cause of, 311
Inhibition of spreaders and differentiation of B. coli and B. aërogenes, 307
Insulin-like material in the tissues of the normal and diabetic animal, 606
  treatment of diabetes, 609
Intestines, biliary exclusion from, 911

J

Jaundice in eclamptic cases, 146
  problems of, and their significance in surgery, 135
Joint tuberculosis, treatment of bone and, 912
Jones, N. W., infection of gall-bladder in relation to pernicious anemia, 469
Joyce, T. M., infection of the gall-bladder in relation to pernicious anemia, 469
Julianelle, L. A., hematological responses to injections of streptococci, 115

K

Kahn, M. H., the human dying heart, 388
  a new vascular sign of death, 890
Kahn reaction in syphilis, 446
Keratosis blennorrhagica from roentgenotherapy, 618
Key, J. A., low back pain, as seen in an orthopedic clinic, 526
Kidney changes in pyloric obstruction, 926
Kilduffe, R. A., utilization of leukocyte counts, 502
Knee-joint, surgery of the, 913

L

Lactic acid milk as a routine feeding for sick and healthy infants, 918
Lange gold-chlorid reaction on the cerebral fluid in infants and young children, 764
Larrabee, R. C., splenectomy, its end-results and clinical indications, 47
Lead in the organism, 779
Leake, C. D., bone marrow and spleen in the treatment of anemia, 819
Leighton, W. E., treatment of tetanus, 852
Leptospira icterohemorrhagiæ in wild rats of Baltimore, 928
Leukemia, a study of mixed, 291
Leukocyte counts, utilization of, 502
Life tables for the population of New York State according to nativity, 928
Lipolds in diabetic bloods, 35
Liver, primary cancer of the, 875

Lobar pneumonia, 293
Loevenhart, A. S., use of tryparsamide in neurosyphilis, 157
Loose bodies arising from articular surface of the joint, 134
Lorenz, W. F., use of tryparsamide in neurosyphilis, 157
Lungs, vital capacity of, 606
Lutz, J. R., observation of fat digestion for clinical study and physiological demonstration, 869
Lyter, J. C., pathways of the mediastinum, the lungs and the pleuræ, 882

M

McLester, tachycardias, prognosis of the, 795
McMillan, T. M., auricular flutter, 893
Malaria, effect of, on the nervous system, 334
Malnourished infants, with a note on the use of insulin, 766
Masson, C. B., effect of malaria on the nervous system, 334
Maternity work among soldiers' wives, 771
Mediastinum, lungs and pleuræ, 882
Meningitis, 142
Mercurochrome, intravenous use of, 916
  ointment in vaginitis, 621
Mesothelium, morphology of the peritoneal, 135
Metabolism of some mineral constituents of cow's milk and of breast milk in the same infant, 452
Mice, resistance of, to transplanted cancer, 780
Miller, J. L., evidence that idiopathic epilepsy is a sensitization disease, 641
Minot, G. R., effect on the blood of irradiation, 215
Mitral stenosis, congenital, 140
Moehlig, R. C., action of suprarenal cortex secretion on mesothelial tissues, 553
Moolten, R. R., non-calculous gallbladder, 684
Mucous colic, so-called, 612
Murphy, W. P., cause of death in diabetes mellitus, 313
Myocardium in non-infectious myocardial failure, 648
Myomectomy, indications for, 148

N

Nasopharynx, absorption of substances, from, 293
Neuhof, S., problems in hypertension, 668
Neurosyphilis, use of tryparsamide in, 157
Newborn, intracranial hemorrhage in, 767
  natural immunization in, 769
  thymus of, 612
Norris, G. W., heart disease, prognosis in organic, 781

O

Obesity and its treatment, 299
Otitis media, 614
Ovary, hypernephroma of, 139

P

Pain as seen in an orthopedic clinic, 526
Pancoast, H. K., herpes zoster in Hodgkin's disease, 326
Pancreatitis, acute, 762
Paratyphoid-enteritidis group, 156
Patients in private practice and the physician's responsibility, 771
Pellagra, treatment and prevention of, 311
Pelouze, P. S., behavior of tuberculous guinea-pigs under parathyroid and calcium administration, 546
Pemphigus, chlorid retention in, 769
Pendergrass, E. P., herpes zoster in Hodgkin's disease, 326
Penetration of normal mucous membranes of the rabbit by treponema pallidum, 466
Peritonitis, primary pneumococcal, 132
Pertussis, diagnosis of, 453
  treatment of, by the roentgen-ray, 141
Phenoltetrachlorphthalein in the study of liver function, 688
Physostigmin and pituitrin, action of, 136
Pleurodynia, or "Devil's grip," 564
Pneumococcus, soluble specific substance of, 778
Pneumonia, treatment of, 915
Poliomyelitis, an immunizing strain of the virus of, 310
Postencephalic behavior disturbances without physical signs, 451
Postmature child, 147
Pregnancy, pyelitis of, 454
  in scurvy in guinea-pigs, 765
  severe disturbance of the heart produced by, 457
  toxemias of, 605
Pucher, G. W., sulphur in treatment of arthritis deformans, 77
Purified Dick scarlatinal toxin, properties of, 926
Pyelitis of pregnancy, 454

R

Radium in treatment of tonsils, 18
Ragweed pollen, 309
Randall, A., antimony compounds for intravenous use, 728
Raw-fruit cure, 612
Rectal digital therapy, 291
surgery, 294
Reeves, W. P., splenic anemia, 836
Reifenstein, B. W., mycotic aneurysm, gonococcal and pneumococcal in origin, 381
Reimann, H. A., sulphur in treatment of arthritis deformans, 77
Reitz, T. F., use of tryparsamide in neurosyphilis, 151
Reviews—
Andrews, Bulloch, Douglas, Dreyer, Gardner, Hildes, Ledingham and Wolf, Diphtheria, 285
Artschwager and Smiley, Dictionary of Botanical Equivalents, 286
Bacon, Obstetrical Nursing, 597
Bandler, Medical Gynecology, 758
Bayly, Venereal Disease, 597
Beck, Diseases of Nose, Throat and Ear, 287
Bickham, Operative Surgery, 440
Bryce, T. H., Ouam's Elements of Anatomy, 438
Buerger, Circulatory Disturbances of the Extremities, 289
Bulletin No. X of the International Association of Medical Museum, 290
Burger, Pathologisch-Physiologische Propädeutik, 287
Bosanquet and Wilson, Pathology and Morbid Anatomy, 126
Cabot, Differential Diagnosis, Vol. II, 285
Campbell, Rommel and Hoffman, Modern Treatment and Medical Formulary, 759
Clendening, Modern Methods of Treatment, 905
Collected Papers of the Mayo Clinic and the Mayo Foundation, 443
Cotton, Dislocations and Joint Fractures, 439
Cowdry, General Cytology, 906
Craig, Diseases of Middle Life, 757
Cushny, Pharmacology and Therapeutics, 437
Dally, High Blood-pressure, 128
Danielopolu, L'Angine de Poitrine, 598
De Lee, Principles and Practice of Obstetrics, 758
Diepgen, Geschichte, 130
Douglas and Priestley, Human Physiology, 600
Reviews—
Du Bois, Basal Metabolism in Health and Disease, 752
Edgell, Theories of Memory, 442
Elias, Jagic and Luger, Bedside Examination, 128
England, First Century of the Philadelphia College of Pharmacy and Science, 902
Faust, Studies on Schistosomiasis Japonica, 439
Fox, Outlines of Medical Hydrology, 288
Fox and Penrose, Disease in Captive Wild Animals and Birds, 754
Gardiner, Handbook of Skin Diseases, 902
Handbook for Mental Nurses, 128
Harrop, Management of Diabetes, 288
Hermann, Methods in Medicine, 129
Hoffstätter, Die Rauchende Frau, 759
Homes, Louis Pasteur, 288
Hornibrook, Culture of the Album, 442
Horowitz, Diabetes, 290
International Medical Annual, 437
Joslin, Diabetic Manual, 284
Kantor Disorders of Digestion, 759
King, Basal Metabolism, 753
Lillie, Protoplasmic Action and Nervous Action, 908
Lindsey, Medical Quotations from English Prose, 753
Luke, Anesthesia in Dental Surgery, 908
McFarland, Surgical Pathology, 603
Mallory and Wright, Pathological Technic, 441
Marlow, Relative Position of Rest of the Eyes and the Prolonged Occlusion Test, 443
Martin, Artificial Limbs, 906
May, Diseases of the Eye, 907
Medical Department of the United States Army in the World War, 903
Montague and Stewart, Pruritus of the Perineum, 127
Moodie, Paleopathology, 444
Morley, Hemorrhoids, 289
Newmayer, Inspection of the Schools for the Health Officer, 284
Norris and Landis, Diseases of the Chest, 438
Ophthalmic Year Book, 1923, Vol. XIX, 129
Pardee, Clinical Aspects of the Electrocardiogram, 907
Petty, Diabetes, 757

Reviews—
Poole, The Avalanche, 752
Porter, Management of the Sick Infant, 598
Practical Medicine Series, Vol. I, 129
Price, Hygiene and Public Health, 437
Radium Report of the Memorial Hospital, New York, 442
Reynolds and Macomber, Fertility and Sterility in Human Marriages, 599
Rossiter, Romance of a Living Temple, 905
Rudolf, Medical Treatment of Disease, 602
de Schweinitz, Diseases of the Eye, 601
Sharp, Foundation of Health, 903
Sharpey-Schafter, The Endocrine Organs, Part I, 286
Simon and Base, Manual of Chemistry, 126
Smith, Essays on the Evolution of Man, 601
Thewlis, Geriatrics, 130
Thomson, Tuberculosis of the Larynx, 285
Thorek, Human Testis and Its Diseases, 904
Tocher, Record of Measurements, Weights and Other Facts Relating to Man, 904
Turner, Diseases of Nose, Throat and Ear, 598
Walters, Domiciliary Treatment of Pulmonary Tuberculosis, 602
Weil, The Internal Secretions, 599
Whiting, Aids to Medical Diagnosis, 290
Whitla, Dictionary of Treatment, 760
Rheumatic fever, pathogenesis of, 463
Roentgen-ray intoxication, 133
studies of stomach function, 615
rays, measurement of the pelvis by, 458
therapy of benign uterine bleeding, 306
Rosenberger, R. C., behavior of tuberculous guinea-pigs under parathyroid and calcium administration, 546
Rothschild, M. A., studies in cholelithiasis, 66
Rudolf, R. D., some cardiac effects of atropin, 641

S

Scarlet fever antitoxin, 461
culture filtrates of hemolytic streptococci from, 463
Scarlet fever, study of hemolytic streptococci associated with, 153
School children, mental health problems in, 915
Schoonmaker, G. D., phenoltetrachlorphthalein in the study of liver function, 688
Sclerosis, coronary, 165
spinal cord and carcinoma of the stomach, 847
Seelig, M. G., diabetes surgery, 495
Serum tetrachlorphthalein test for liver function, 606
Sheppard-Towner act, 922
Silver arsphenamin, action of, 769
Sleep, loss of, effect on composition of blood and urine, 151
Small, J. C., protozoan organism within erythrocytes of patients suffering from pleurodynia, 570
Smith, C., treatment of tetanus, 852
Sodium citrate, effects of injection of, upon bleeding, 607
Splenectomy, 47
Spondylolisthesis, 295
Sporotrichosis in the rat, 144
Spotted fever, immunity in Rocky Mountain, 780
Spurling, R. G., effect on the blood of irradiation, 215
Stenosis, pyloric, in infants, 296
Stern, L. D., sclerosis of the spinal cord and carcinoma of the stomach, 847
Stetson, R. E., blood transfusion, 534
Streptococcus hemolyticus in scarlet fever, 308
Stricture of female urethra, 150
Sulpharsphenamin in Vincent's angina and stomatitis in children, 450
Sulphemoglobinemia, 89
Sulphur in treatment of arthritis deformans, 77
Suprarenal cortex, action of, on mesothelial tissues, 553
Suprarenin in clinic and practice, 298
Sweeney, J. A., auricular flutter, 893
Syphilis as a complication of pregnancy in the negro, 770
congenital, results in treatment of, 614, 777
diagnosis and treatment of, 136
as a factor in the etiology of mental deficiency, 465
from an experimental point of view, 919
primary and secondary, 697
treatment, results in, 921
Syphilitics, spinal fluid in, 144

T

Tachycardias, prognosis of the, 795
Temperature and blood concentration in the newborn with fever, 453

Tendon of Achilles, tenotomy of the, 912
Tetanus, treatment of, 852
Thomas, B. A., primary and secondary syphilis, 697
Thyroidectomized sheep, pathological changes in, 927
Thyroid treatment of the nephroses, 611
Tonsillectomy, effect of, on the general health, 451, 605
Torrey, R. G., epidemic diaphragmatic pleurodynia, or "Devil's grip," 564
Toxemia of pregnancy, 302, 605
cerebral symptoms produced by, 304
treatment of, 613
Tuberculosis in infancy, 704
pulmonary, 1
studies on the relation of mineral dusts to, 154
surgery of pulmonary, 268, 412, 574
Tumor susceptibility and heredity, 467
Typhoid fever and ice, 779
saline vaccine, 151

U

Ulcer, duodenal, among medical men, 135
Ultraviolet light, skin resistance to, 617
Ureteral catheterization, 623
Urinary bladder, reactions of, in canine anaphylaxis, 308
Use of diphtheria antitoxin, 467
Uterine fibroids, surgical treatment of, 774
treatment of, 925
prolapse, operation for, 150
operative treatment of, 459
secretion, nature of, 619
treatment of, 622

V

Vaccinations, protection against typhoid-like, by, 152
Venereal disease, relation of, to childbirth, 923
Venous pressure, 761
Vesical distention, 133
Virus of poliomyelitus, activity of, 466
Vitamin C, lack of, on resistance of the guinea-pig of bacterial infection, 465
Vogel, K., sulphemoglobinemia, 89

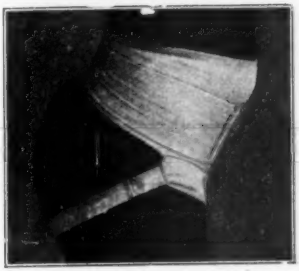
W

Wachowiak, M., relation of Fungi imperfecti to diarrheal conditions, 371
Wilensky, A. O., studies in cholelithiasis, 66
Williams, F. H., radium radiations in treatment of tonsils, 18
Willius, F. A., coronary sclerosis, 165
Wilson's disease in infancy, 140
Winkelstein, A., pressure factors in the biliary duct-system of the dog, 812
Woolstein, M., tuberculosis in infancy, 704

Trademark Registered **STORM** Trademark Registered

Binder and Abdominal Supporter

(Patented)



Trade Mark Reg. Trade Mark Reg.

For Men, Women and Children

For Ptosis, Hernia, Pregnancy, Obesity, Relaxed Sacro-iliac Articulations, Floating Kidney, High and Low Operations, etc.

Ask for 36-page Illustrated Folder
Mail orders filled at Philadelphia only—within 24 hours

Katherine L. Storm, M.D.

Originator, Patentee, Owner and Maker

1701 DIAMOND ST. PHILADELPHIA

D=Zerta

A Sugar-Free Dessert

FOR

Diabetic Conditions

WRITE TO

The Jell-O Company, Inc.

LE ROY, N. Y.

F. & R.'s
GENUINE
GLUTEN FLOUR

Guaranteed to comply in all respects to standard requirements of the U. S. Department of Agriculture.

Manufactured by
THE FARWELL & RHINES CO.
Watertown, N.Y., U.S.A.

Calcreose

In Bronchitis and Tuberculosis

Calcreose is particularly suitable as an adjunct to other remedial measures. **Calcreose** contains 50% creosote in combination with calcium. **Calcreose** has all the pharmacologic activity of creosote but is apparently free from untoward effects even when taken in large doses for long periods of time.

Sample 4 grain tablets supplied to physicians upon request

THE MALTBIE CHEMICAL CO., NEWARK, N. J.

"A Safe and Desirable Beverage"

IN SUMMING up the results of his three years' Scientific Coffee Research at the Massachusetts Institute of Technology, Professor Samuel C. Prescott says—

"I will say that neither in the dispassionate study of the vast literature on the subject, much of which is medical literature, nor as a result of our long-continued studies, have we been forced as scientific men to any conviction that well-made Coffee is harmful to the great mass of consumers and, as such, dangerous to public health and welfare.

"On the contrary, the more deeply we have gone into this matter, the more we have read, the more we have looked up this literature in different languages, the more firmly fixed has become the belief (*in fact, I might say it is a belief so strong that it is a conviction*) that for the overwhelming majority of adults Coffee is a safe and desirable beverage."

A complete copy of Professor Prescott's address on the results of his three years' Scientific Coffee Research will be mailed to physicians on request.

Joint Coffee Trade Publicity Committee, 64 Water Street, New York, N. Y.

Announcing

A NEW PRODUCT

Nujol

REG. U.S. PAT. OFF.

with

AGAR

At the suggestion of a number of our friends in the medical profession who prefer in certain cases to prescribe Liquid Petrolatum in the form of an emulsion, we are presenting for your attention — Nujol emulsified with Agar. This product is intended for prescription use only.

Our Research Laboratories have been working for a considerable time to perfect Nujol with Agar. And rigid tests have demonstrated that in quality, suitability and purity it is unsurpassed.

Nujol with Agar is a perfect emulsion. It contains no cathartic ingredient, its action being entirely mechanical. Moreover, its creamy smoothness and pleasant flavor render it highly palatable, particularly to children.

Test Nujol with Agar yourself. A sample will be sent you on request.

Made by the makers of

Nujol

Nujol Laboratories

STANDARD OIL CO. (NEW JERSEY)

7 Hanover Square, New York

Information Regarding Karo Syrup

(THE CORN SYRUP NOW BEING PRESCRIBED FOR INFANT FEEDING)

KARO SYRUP is the ideal Dextrose-containing agent for all classes, ages and conditions of people, but peculiarly so for those whose starch and sugar-converting functions are either in partial or more or less complete abeyance.

As a quickly and completely available form of converted carbohydrate and as a nutritive element of decided potency and universal tolerability, KARO SYRUP is a distinctly valuable addition to the diet of either child or adult requiring heat and energy-producing, readily oxidizable pabulum.

KARO SYRUP is the ideal sugar supplier for the infant, the older child, the adolescent and for such among the adults as may require a reinforcement of carbohydrate or sugar nutrition.

NOTE: There are three kinds of Karo —Red Label, Blue Label and Orange Label. The nutritive value and digestibility of all three are practically equal.

Used with **Insulin** Treatment

White enamel with porcelain (acid proof) top and washable dial that always remains white and legible—never turns brassy or green.

HANSON

Dietetic Scale

ACCURATE and easy to use. Place empty plate on platform and rotate dial until "O" is under end of pointer. Place food on plate until proper amount in grams is registered. Rotate dial again until "O" is under end of pointer, and weigh another article of food. Repeat process until all the foods called for in dietetic prescription have been correctly weighed. Tare is automatically deducted.

CAPACITY, 500 GRAMS BY 2 GRAMS

Secure this scale from any reputable supply house or direct from us

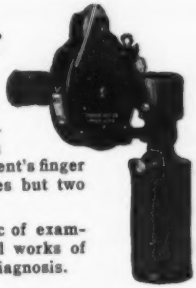
Price to consumers, $11
Price to hospitals and physicians, $10

HANSON BROTHERS SCALE COMPANY

Established 1888

535 North Ada Street - - Chicago

Hemoglobinometer Dare Aluminum



Blood is examined undiluted. Complete operation from the puncturing of patient's finger to cleansing of pipets takes but two minutes.

The application and technic of examination are described in all works of Hematology and Clinical Diagnosis.

Rieker Coagulometer

BRODIE-RUSSELL-BOGGS PATTERN

Most accurate and quickest method for determining coagulative quality of the blood.

For sale by all Supply Houses

Write for descriptive circulars

RIEKER INSTRUMENT COMPANY
1919 Fairmount Avenue Philadelphia

Ready to take an invigorating bath in the curative waters of Virginia Hot Springs.

Prescribe a Winter Rest at Virginia Hot Springs!

THE rush and bustle of the winter season—business worries—social activities—these are the things that bring patients to you every year—tired and nervous but not seriously ailing. You know the cure is a rest—a rest at some refreshing place—a rest at Virginia Hot Springs.

It offers everything. Up 2400 feet above sea level—in a beautiful mountain-surrounded valley—with clear, dry air and loads of sunshine. A pleasant place for lolling—and a pleasant place for sports.

And advise your patient to take the famous spa Cure. Given according to your instructions, under the supervision of a physician. Baths — heated-air treatments — massage and Zander. Relaxing and invigorating!

A few weeks at Virginia Hot Springs will make a new person out of your nerve-wracked patient — and moreover, he'll enjoy every minute of his stay—and that's important, too!

Send for special literature for physicians. Analysis of spas —reports of cure cases—etc.

Virginia Hot Springs
The HOMESTEAD

Christian S. Andersen, Res. Mgr.

Hot Springs - Virginia

Convalescing in the pleasantest possible way in the sunny luxury of The Homestead.

THE STANDARD

LOESER'S INTRAVENOUS SOLUTIONS

CERTIFIED

SODIUM THIOSULPHATE

For arsphenamine dermatitis, arsenic, mercury and other metallic poisoning, dermatitis of organic origin.

Loeser's Intravenous Solution of Sodium Thiosulphate, 10 c.c. contain 1 gram (15 grains) of Sodium Thiosulphate U. S. P., a 10% solution.

Loeser's Intravenous Solutions
ARE THE
Standardized, Certified Solutions

Send for Literature, Price Lists, and The "Journal of Intravenous Therapy"

NEW YORK INTRAVENOUS LABORATORY
100 West 21st Street New York, N. Y.
Producing ethical intravenous solutions for the medical profession exclusively

Toxemia

In the poisoning of the body by toxins in infectious disease, the most destructive effect is upon the nerve cell tissues, resulting in marked depression of the nervous system. In such conditions

ESKAY'S NEURO PHOSPHATES

will be found most helpful, stimulating nerve cell function, restoring nerve cell tonicity, and greatly accelerating the process of convalescence.

SMITH, KLINE & FRENCH CO.
105-115 N. 5th St., Phila., Pa.
Established 1841
Manufacturers of
Eskay's Food

An Invitation to Physicians

Physicians in good standing are cordially invited to visit the Battle Creek Sanitarium and Hospital at any time for observation and study, or for rest and treatment.

Special clinics for visiting physicians are conducted in connection with the Hospital. Dispensary and various laboratories.

Physicians in good standing are always welcome as guests, and accommodations for those who desire to make a prolonged stay are furnished at a moderate rate. No charge is made to physicians for regular medical examination or treatment. Special rates for treatment and medical attention are also granted dependent members of the physician's family.

An illustrated booklet telling of the Origin, Purposes and Methods of the institution, a copy of the current "MEDICAL BULLETIN," and announcements of clinics, will be sent free upon request.

THE BATTLE CREEK SANITARIUM **Room 221** **Battle Creek, Michigan**

NOVASUROL

Trademark Reg. U. S. A. Pat. Off.

Brand of **MERBAPHEN**

The Dependable Diuretic In Cardiorenal Dropsies:

When every other remedy fails in serious cardiorenal conditions a single injection of Novasurol often induces prompt and profuse diuresis with subsidence of edema.

The Improved Mercurial Injection for Syphilis:

Novasurol is preferred by many syphilologists to other soluble mercurials, because of its high content of mercury but low toxicity, general painlessness of injections, prompt and prolonged action. It can be injected alone or mixed with arsphenamin.

HOW SUPPLIED: 1.2 c. c. ampules, in boxes of 5.

Pamphlet on Request

WINTHROP CHEMICAL COMPANY, Inc., 117 Hudson St., New York, N. Y.

The ADRENALIN *Group*

WHEN you specify "Adrenalin, P. D. & Co." in your prescriptions or orders, you give your patient the benefit of more than twenty years of manufacturing experience with the pressor principle of the suprarenal gland, discovered by Takamine in 1900 and placed upon the market by Parke, Davis & Company in 1901.

Adrenalin is a life-saver in more senses than one. Its effect upon the arterial system and the heart is phenomenally swift and potent; while for antiphlogistic effect on the inflamed mucosa in nasal, laryngeal, rectal and genito-urinary conditions, it is unexcelled. Invaluable in shock, collapse, serum rash, and to control operative hemorrhage. The one reliable symptomatic remedy for asthma.

Among our Adrenalin preparations the following deserve to be constantly kept in mind:

ADRENALIN INHALANT (1:1000)

Indicated in acute, subacute or chronic rhinitis, pharyngitis, tonsillitis, laryngitis; in scarlatinal angina, and in hay fever. A pronounced astringent.

ADRENALIN OINTMENT (1:1000)

Used for the same purpose as the Inhalant, and in urethritis for its astringent effect. A serviceable lubricant for urethral instruments.

ADRENALIN SUPPOSITORIES (1:1000)
ADRENALIN AND CHLORETONE SUPPOSITORIES

In hemorrhoids, proctitis, rectal pruritus, or rectal fissure, these suppositories are very serviceable. Cone-shaped; melt at body temperature. Insert one suppository at night and one in the morning.

Write us for booklet, "Adrenalin in Medicine."

PARKE, DAVIS & COMPANY

Included in N. N. R. by the Council on Pharmacy and Chemistry of the A. M. A.

PRESCRIBE

The Original

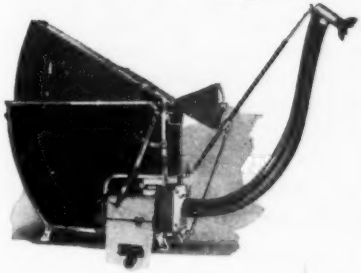
Nourishes — Invigorates — Sustains
Assimilated by the weakest system

Avoid imitations

Samples upon request

Horlick's Malted Milk Co.
RACINE, WIS.

McKESSON
METABOLOR
Recording



Makes metabolism tests as easy and as accurate as a blood count

Ask for Details

TOLEDO TECHNICAL APPLIANCE CO.
Toledo, Ohio

THE GLEN SPRINGS
WATKINS GLEN, N. Y.
ON SENECA LAKE

Situated in the beautiful Finger Lakes region of New York State; clear, dry, invigorating atmosphere.

OPEN THE YEAR ROUND

RHEUMATISM

The Glen Springs offers complete facilities for the scientific treatment of rheumatism. And, with its facilities for the treatment of heart disorders, it is prepared to receive patients suffering from rheumatism complicated with heart lesions.

These facilities include:

Concentrated hot brine baths of high specific gravity which give up heat readily and induce perspiration; fomentation, bakes, packs, cabinets, leucodescent light, approved modern electrical appliances and massage.

The treatments are prescribed and supervised by skilled physicians. Complete X-ray equipment for diagnosis and assistance in watching progress of conditions. The closest coöperation between the professional personnel at The Glen Springs and the patient's home physician is always maintained.

Illustrated and detailed booklets prepared especially for the Medical Profession on request

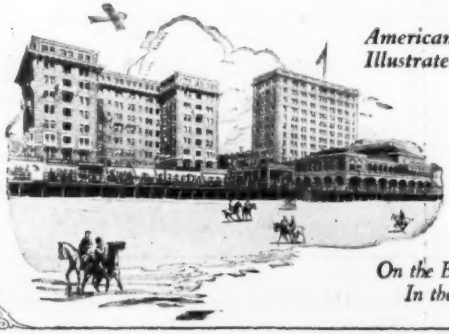
William E. Leffingwell, President

CHALFONTE-HADDON HALL
ATLANTIC CITY

Fall and Winter Outdoors:

GOLF
RIDING
ON THE BEACH
BOARDWALK
ACTIVITIES
AVIATION

Every season of the year is enjoyable at these two delightful hotels on the Boardwalk. During the winter of December, 1923, January and February, 1924, they entertained an average of 598 guests *each day.* Whether you take time off in Winter or Summer, Spring or Autumn, you will always find healthful recreation and rest at hospitable, home-like Chalfonte-Haddon Hall.



American plan only. Always open.
Illustrated folder and rates on request.

LEEDS and LIPPINCOTT COMPANY

On the Beach and the Boardwalk
In the very center of things

Only Heroic Measures will

Save the Pregnant Woman

who is anuric or in convulsions. Give her the undisputed benefits of alkali by starting its administration early.

Patients do not tire of drinking KALAK WATER as they do of other methods of taking alkali.

Each bottle carries in sparkling form several grammes of the bicarbonates of sodium, potassium, calcium and magnesium.

Kalak Water Company
6 Church Street
New York City

OSLER and McCRAE'S

MODERN MEDICINE

A New Third (3d) Edition of this Epochal Work is in Active Preparation

EDITED BY

THOMAS McCRAE, M.D.

Professor of Medicine in the Jefferson Medical College, Philadelphia

First volume ready about January, 1925

WRITE FOR PROSPECTUS

S. Washington Sq. LEA & FEBIGER Philadelphia

What would you give to avoid tuberculosis?

YOU would give everything you have to avoid the Great White Plague. The germs of tuberculosis are everywhere. There is only one sure way for you and everybody to avoid consumption, and that is to stamp out the disease entirely.

It can be stamped out. Today only one person dies of tuberculosis where two died before. Christmas Seals helped to save the other life.

The war against tuberculosis, waged by the Tuberculosis Associations, is financed by the annual sale of Christmas Seals. Remember, when you buy Christmas Seals, you not only help to save others, but you protect yourself as well. Buy Christmas Seals—and buy as many as you can.

STAMP OUT
TUBERCULOSIS
WITH
CHRISTMAS
SEALS

A group of children taking the sun cure to avoid tuberculosis

THE NATIONAL, STATE, AND LOCAL TUBERCULOSIS ASSOCIATIONS OF THE UNITED STATES

GRAY'S ANATOMY

New (21st) Edition

THOROUGHLY REVISED AND RE-EDITED BY

WARREN H. LEWIS, B.S., M.D.

Professor of Physiological Anatomy, Johns Hopkins University, Baltimore;
Research Associate, Carnegie Institution of Washington

Imperial Octavo, 1417 Pages with 1283 Large and Elaborate Engravings
Cloth, $10.00, net

ON ITS ORIGINAL APPEARANCE, *sixty-six years ago*, it immediately took the leading place, and it has not only maintained its position in its own subject, but has also become the *best-known work in all medical literature in the English language.* It is incomparably the greatest text-book in medicine, measured by the numbers of students who have used it, and it is unique also in being the one work which is certain to be carried from college to afford guidance in the basic questions underlying practice.

The special sections on Embryology and Histology are, as in the previous edition, distributed among the subjects with which they naturally belong. This arrangement emphasizes the unity of the three great divisions of human anatomy—*embryology, microscopic anatomy and gross anatomy*—and the advantage of their coördinate study for the best understanding of the human body. Every section has been brought up to date, conspicuous for their wealth of new material being those on the architecture of the Heart Musculature, Embryology and the Ductless Glands. Special attention is called also to the matter on the Nervous System, the central connections of the Spinal and Cranial Nerves, Physiological Anatomy, Laws of Bone Architecture, Mechanics and Variations of Muscles and the rational presentation of the Sympathetic Nervous System.

Illustrations—always an outstanding feature of Gray—have been added generously, and throughout the work colored pictures have been used *even more extensively* than heretofore. The names of the parts are engraved, wherever possible, directly on the illustrations. *Thus the nomenclature, positions, extent and relations of the parts are seen at a glance.* The use of the B. N. A. nomenclature in English is employed and important references to the literature have been added at the end of each section. A superb index completes all the service which it is possible for a book to render. The new *Gray* reflects all the latest accessions to anatomical knowledge and embodies all that careful thought and unstinted expenditure can combine in a text-book. *The price remains the same.*

MANUAL OF SURGICAL ANATOMY

By

ALBERT C. EYCLESHYMER, Ph.D., M.D.
Dean, College of Medicine, University of Illinois; Professor and Head of Department of Anatomy, Histology and Embryology

and

TOM JONES, B.F.A.
Artist and instructor, Department of Anatomy, Histology and Embryology, University of Illinois

IN PREPARATION. READY SOON

S. WASHINGTON SQUARE **LEA & FEBIGER** PHILADELPHIA

Just off Press

BASAL METABOLISM IN HEALTH AND DISEASE

By EUGENE F. DU BOIS, M.D.

Medical Director, Russell Sage Institute of Pathology; Associate Professor of Medicine, Cornell University Medical College

Octavo, 372 pages with 79 engravings. Cloth, $4.75, net

BASAL METABOLISM has become of considerable importance. Most of the literature which deals with it, however, is written primarily for research workers or physiologists. *This book brings basal metabolism out of the realm of pure physiology into the domain of clinical medicine.* It is written for physicians and surgeons, students, physiologists and for dietitians.

The development of ten years' work with the only respiration calorimeter which measures heat by the direct and indirect methods established in a hospital, the book views the subject from the standpoint of the physiologist and the practical clinician.

It is far more than a mere discussion of basal metabolism, since it deals with the fundamentals of the science of metabolism and the basis of all dietaries. Dr. Du Bois discusses the metabolism of protein, fat and carbohydrate in health and disease, also the general principles which must be applied to all dietaries. Indeed this book might also be called "FUNDAMENTAL PRINCIPLES OF DIETETICS."

Part I (8 chapters) considers metabolism in Health—Physics, Gases, Apparatus, Technic, Calculations, Surface Area, etc. Part II (11 chapters) is devoted to the thorough consideration of Metabolism in Disease.

Principles of Biochemistry

For Students of Medicine, Agriculture and Related Sciences

By T. BRADSFORD ROBERTSON, Ph.D., D.Sc.

Professor of Physiology and Biochemistry, University of Adelaide, South Australia; Formerly Professor of Biochemistry, University of Toronto; Professor of Biochemistry and Pharmacology, University of California

New (2d) Edition. Octavo, 796 pages with 57 engravings. Cloth, $8.50, net

THIS EDITION is 163 pages larger than the preceding, a number of changes and a considerable amount of new matter having been incorporated. These have been rendered necessary by the advances in our knowledge, and, in part, have been indicated by the experience gained in the employment of the book as a text for students of medicine and science. Many suggestions received from friends and reviewers have also been adopted.

Almost every chapter has undergone considerable revision. The sections dealing with the regulation of the NEUTRALITY of the BLOOD, with COLLOIDS, and with METABOLISM in DIABETES have been much expanded by the incorporation of new material and fuller treatment of the old. The chapter on GROWTH has been almost entirely rewritten and a *new chapter* has been added on the RELATIONSHIP of GROWTH to DIET. *New Sections* have been added dealing with RACEMIZED PROTEINS, the FUNCTIONS of the NUCLEIC ACIDS and the INCLUSION of the ENVIRONMENT as a FACTOR in the EVOLUTION of the HIGHER ANIMALS.

S. Washington Square **LEA & FEBIGER** PHILADELPHIA

Have You These NEW BOOKS and EDITIONS?

MODERN UROLOGY
Edited by HUGH CABOT, M.D. *New (2d) Edition.* Two octavo volumes, totalling 1572 pages with 686 engravings and 19 plates.
Cloth, per set, $18.00, net.

TREATMENT of DIABETES MELLITUS
By ELLIOTT P. JOSLIN, M.D. *New (3d) Edition.* Octavo, 784 pages, illustrated. *Cloth, $8.00, net.*

DIABETIC MANUAL
By ELLIOTT P. JOSLIN, M.D. *New (3d) Edition.* 12mo, 211 pages, illustrated. *Cloth, $2.00, net.*

PHARMACOLOGY and THERAPEUTICS
By ARTHUR R. CUSHNY, M.D. *New (8th) Edition.* Octavo, 707 pages with 73 engravings.
Cloth, $6.00, net.

MANUAL of PROCTOLOGY
By T. CHITTENDEN HILL, M.D., Harvard Graduate School of Medicine. *New.* 12mo, 280 pages with 84 engravings. *Cloth, $3.25, net.*

ELEMENTARY ANATOMY and PHYSIOLOGY
By MARY REES MULLINER, M.D. Octavo, 367 pages with 301 engravings in black and colors.
Cloth, $4.50, net.

Modern Aspects of THE CIRCULATION in HEALTH and DISEASE
By CARL J. WIGGERS, M.D. *New (2d) Edition.* Octavo, 662 pages, 204 engravings.
Cloth, $7.50, net.

BRAUN'S LOCAL ANESTHESIA
Translated from Sixth German Edition and Edited by MALCOLM L. HARRIS, M.D., Chicago Policlinic. Octavo, 411 pages with 231 illustrations in Black and Colors. *Cloth, $5.00, net.*

OBSTETRICAL NURSING
By CHARLES S. BACON, University of Illinois and Chicago Policlinic. *New (2d) Edition.* 12mo, 340 pages with 126 illustrations.
Cloth, $2.75, net.

HYGIENE and PUBLIC HEALTH
By GEORGE M. PRICE, M.D. *New (3d) Edition.* 12mo, 306 pages. *Cloth, $2.25, net.*

Medical and Sanitary INSPECTION OF SCHOOLS
By S. W. NEWMAYER, M.D. *New (2d) Edition.* 12mo, 462 pages with 79 engravings and 6 plates.
Cloth, $4.00, net.

GREEN'S Manual of PATHOLOGY and MORBID ANATOMY
Revised by W. C. BOSANQUET, M.D., and G. S. WILSON, M.D., Charing Cross Hospital, London. *New (13th) Edition.* Large 12mo, 624 pages, 244 engravings, 6 colored plates.
Cloth, $7.50, net.

THE DIETARY of HEALTH and DISEASE
By GERTRUDE THOMAS, University of Minnesota. *New.* 12mo, 210 pages, illustrated.
Cloth, $2.25, net.

ORTHOPEDIC SURGERY
By ROYAL WHITMAN, M.D. *New (7th) Edition.* Octavo, 993 pages with 877 engravings.
Cloth, $9.00, net.

DISEASES of the SKIN
By FRANK CROZER KNOWLES, M.D. *New (2d) Edition.* Octavo, 595 pages, 229 engravings, 14 plates. *Cloth, $6.50, net.*

Manual of CHEMISTRY
By W. SIMON, M.D., and DANIEL BASE, PH.D. *New (12th) Edition.* Octavo, 667 pages, 55 engravings, 7 colored plates. *Cloth, $5.00, net.*

NUTRITION and CLINICAL DIETETICS
By H. S. CARTER, M.D., P. E. HOWE, PH.D., and H. H. MASON, M.D. *New (3d) Edition.*
Cloth, $7.50, net.

INDIVIDUAL GYMNASTICS
By LILLIAN C. DREW. *New (2d) Edition.* 12mo, 260 pages, 109 engravings.
Cloth, $2.00, net.

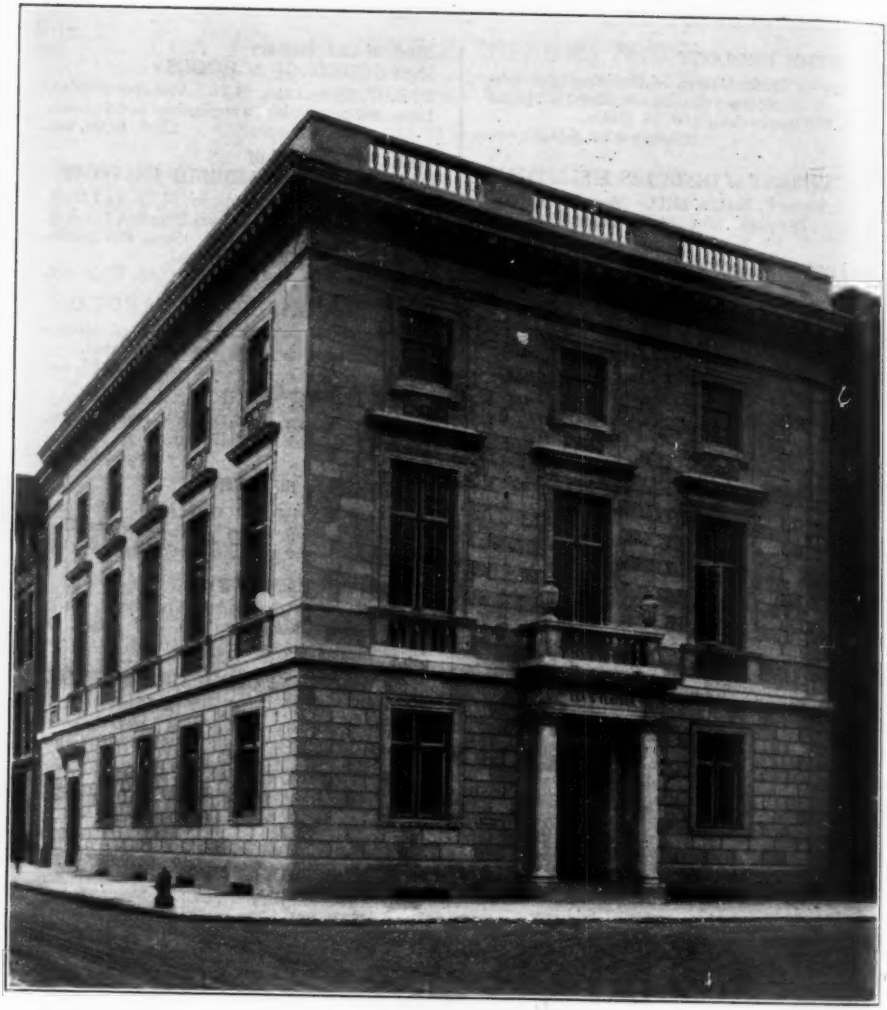
FUNDAMENTALS OF BACTERIOLOGY
By CHARLES B. MORREY, M.D. *New (3d) Edition.* 12mo, 344 pages, with 171 engravings and 6 plates. *Cloth, $3.50, net.*

QUALITATIVE CHEMICAL ANALYSIS
By THEO. J. BRADLEY, A.M., PH.G. *New (3d) Edition.* 12mo, 173 pages. *Cloth, $2.50, net.*

APPLIED ANATOMY and KINESIOLOGY
By WILBUR BOWEN. *New (3d) Edition.* Octavo, 352 pages, 217 engravings. *Cloth, $3.75, net.*

LEA & FEBIGER

SOUTH WASHINGTON SQUARE PHILADELPHIA



New Building of

Washington Square LEA & FEBIGER Philadelphia

1785 *One Hundred and Forty Successful Years* 1924

ON THE opposite page is shown the new building of LEA & FEBIGER, at the corner of Sixth Street and South Washington Square, Philadelphia. It is the newest of a number of fine modern buildings that now adorn the square on all sides. The style of architecture is the Italian *renaissance*, and the building is finished in white stone which lends itself very well to this type of architecture. Constructed entirely of reinforced concrete, brick and stone, it is fireproof throughout. Here are located the general offices, stock and shipping departments, also a spacious lobby and reading room for the convenience of visiting physicians. No manufacturing is done here, the printing plant, bindery and warehouse being separate units.

The occupancy of this new building marks the beginning of a new era in the history of this firm, which now spans three centuries. The business dates back nearly to the close of the Revolutionary War, being established in 1785, and thus antedates the Constitution of the United States by four years. It has been in continuous operation ever since, has withstood the vicissitudes of almost a century and a half, and through the many alternations of peace and war, prosperity and depression, has invariably maintained its commercial honor and never failed to meet its obligations to the day.

In the early days the firm gave its attention to general literature, and published Wemyss' biographies of Washington and Marion, Jefferson's "*Notes on Virginia*," and (in this country) the Waverly Novels, the works of Dickens, of Washington Irving, the novels of Fenimore Cooper, the "*Encyclopedia Americana*," and other famous books. For the greater part of its existence, however, it has specialized in Medicine. For sixty-six years it has been the publisher in America for *Gray's Anatomy*, the most famous work in all medical literature and the one which has been termed "The Bible of Medicine." It is also interesting to note that *The American Journal of the Medical Sciences* is now in its one hundred and fifth year of continuous publication, having been established in 1820.

With greatly enlarged facilities of the most modern type, the firm confidently looks forward to an even greater increase in the volume of its business than in recent years, gratifying as that has been. It has always been a source of great satisfaction to the firm that the extension of its business meant likewise the extension of knowledge. It has always entertained a high sense of respect for its own imprint, and has felt a just pride in the belief that its name on a title page is an indication of the worthiness of the volume in which it appears. For a continuation of the prosperity which has now, for one hundred and forty years, never failed to accompany the operations of the house, the firm relies upon a maintenance of its tradition of honorable dealing and unflagging industry, and upon what has been its greatest asset throughout its entire history—*the Good Will of the Medical Profession*.

Washington Square **LEA & FEBIGER** Philadelphia

INDEX TO ADVERTISERS

TO OUR SUBSCRIBERS—only ethical products of the highest quality can be advertised in this Journal. The firms listed below merit your full confidence, all are recognized leaders in their fields. Will you kindly mention THE JOURNAL when writing them? Thank you.

Apparatus and Instruments

(Colorimeters, Haemacytometers, Hemoglobinometers, Microscopes, Sterilizers, Bacteriological Supplies, etc.)

PAGE

Castle, Wilmot, Co. 7
Hynson, Westcott & Dunning 20
E. Leitz, Inc. ....
Merck & Co 16
Rieker Instrument Co. 25
Arthur H. Thomas Co. 3
Wilmot Castle Co. 7

Binders, Supporters, etc.

Katherine L. Storm, M.D. 21

Basal Metabolism Apparatus

Arthur H. Thomas Co. 3
Toledo Technical Appliance Co. 29

Blood Pressure Apparatus

W. A. Baum Co. ....
Becton, Dickinson & Co. 40

Biologicals, Drugs and Pharmaceuticals

Abbott Laboratories 7
Arlington Chemical Co. 15
E. Bilhuber, Inc. 14
Calco Chemical Co. 5
G. W. Carnrick Co. 11
Ciba Co. ..... 4th Cover
Deshell Laboratories 9
Fairchild Bros. & Foster 5
Hoffmann-LaRoche Chemical Works 6
Hynson, Westcott & Dunning 20
Intra Products Co. 18
Lavoris Chemical Co. ....
Lederle Antitoxin Laboratories 20
Eli Lilly & Co. 1
Maltbie Chemical Co. 21
Merck & Co. 16
H. K. Mulford Co. 13
National Aniline & Chemical Co. 18
New York Intravenous Laboratory 26
Nujol Laboratories 23
Parke, Davis & Co. 28
Schering & Glatz, Inc. 19
Sharp & Dohme ..... 2d Cover
F. A. Upsher Smith 4
Smith, Kline & French 26
Winthrop Chemical Co. 27

Chlorine Apparatus

Wallace & Tiernan 8

Electrical Diagnostic Instruments

Electro Surgical Instrument Co. 15

Electrocardiographs

Cambridge Instr. Co. 18

Foods, Beverages, etc.

Borcherdt Malt Extract Co. ..... 3d Cover
Célestin's Vichy 6
Corn Products Co. 24
Farwell & Rhines 21
The Fleischmann Co. 2
The Jell-O Co. 21
Joint Coffee Trade 22
Horlick's Malted Milk Co. 29
Laboratory Products Co. 39
Lister Bros., Inc. 13
Mellin's Food Co. ..... 4th Cover

Acidophilus Milk

Lederle Antitoxin Laboratories 20

Malt Sugar

Borcherdt Malt Extract Co. ..... 3d Cover

Radium

Radium Chemical Co. ....

Radium Emanation

Radium Emanation Corp. ..... 3d Cover

Resorts and Hotels

Battle Creek Sanitarium 27
Chalfonte-Haddon Hall 30
The Glen Springs 29
The Homestead, Hot Springs, Va. 25

Scales (Dietetic and Nursery)

Hanson Bros. 25

Sutures and Ligatures

Davis & Geck, Inc. ..... 2d Cover

Syringes, Needles and Thermometers

Becton, Dickinson & Co. 40

X-Ray Apparatus, Tubes, etc.

Victor X-Ray Corp. 17

Miscellaneous

Kalak Water Co. 31
Lea & Febiger 31–37

THE EXPERIENCE

of thousands of physicians is constantly confirming the fact that S. M. A. may be relied upon to give excellent nutritional results in the great majority of cases. Physicians have the additional assurance that S. M. A. prevents rickets and spasmophilia.

Literature and samples sent promptly on request

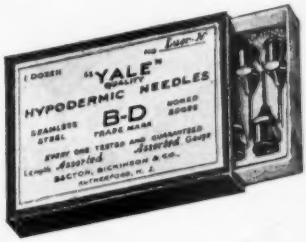
THE LABORATORY PRODUCTS CO.
Cleveland, Ohio

B-D PRODUCTS

Made for the Profession

Have you noticed that these two products function best together?

Genuine Luer Syringes and Yale-Luer Needles always fit perfectly.



Made in the same plant, measured by the same micrometer gauge, and guaranteed to fit—Genuine B-D Luer Syringes and Yale Quality Needles give satisfactory service when used *together*.

It is only logical that the superintendent of a leading Boston hospital states:

> "Our experience has shown us that since we standardized on B-D Luer Syringes and Yale Needles, the Hospital has actually saved money and derived more satisfactory results than when we were buying various makes of syringes and needles."

Add to these facts the annealing, the careful grinding by hand, the rigid inspection and testing of B-D Luer Syringes —with the individual grinding, honing, and testing of Yale Needles—and it is easy to see why these two products are most *economical* and *dependable*.

For your protection, Genuine B-D Products are marked B-D

INSIST UPON THE GENUINE

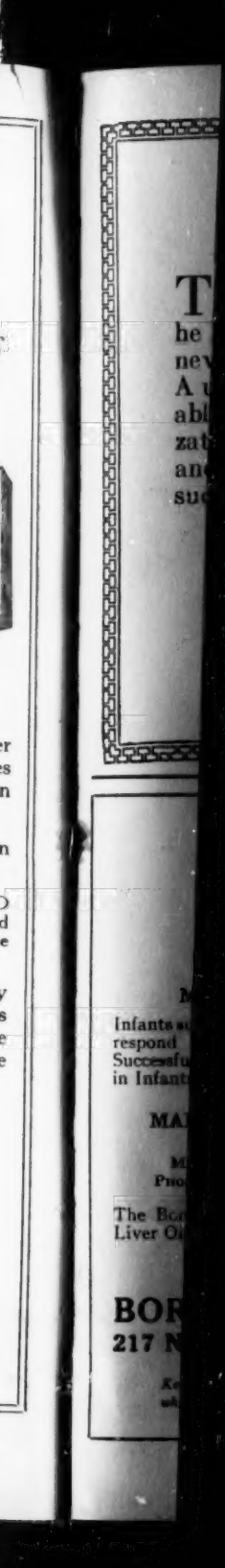
Supplied through dealers

BECTON, DICKINSON & CO.

RUTHERFORD, N. J.

Makers of Genuine Luer Syringes, Yale Quality Needles, **B-D** *Thermometers, Ace Bandages, Asepto Syringes, Sphygmomanometers and Spinal Manometers*

JUN 20



oducts

icrometer
Syringes
ice when

g Boston

d on B-D
lly saved
we were

ding by
yringes
of Yale
ucts are

eters,
eters

RADIUM EMANATION (RADON) SERVICE

THE SURGEON finds here just the sort of a service he has always felt ought to exist, even though he has never found it.

A utility which when added to his armamentarium enables him to widen his range of treatment. An organization that knows his needs, understands his problems and is ever ready to cooperate to make his results successful.

Literature on request.

THE RADIUM EMANATION CORPORATION
250 WEST FIFTY-SEVENTH STREET
NEW YORK CITY
Telephone Circle 3649

SERVICE RADON

Strictly American Products
of Dependable Character

BORCHERDT'S

MALT SOUP EXTRACT

Infants suffering from marasmus and atrophy respond quickly to Malt Soup Therapy. Successfully used in correcting constipation in Infants.

MALT SUGAR

MALTOSE 87.4%. DEXTRIN 4.35%

The only Malt Sugar on the market without large admixtures of Dextrins

MALT COD LIVER OIL AND PHOSPHORUS

MALT 75%. COD LIVER OIL 25%
PHOSPHORUS $\frac{1}{75}$ GR. IN FLUID OUNCE

MALT COD LIVER OIL AND IRON IODIDE

MALT 75%. COD LIVER OIL 25%
IRON IODIDE 4 GR. IN FLUID OUNCE

These products are entirely free from alcohol.

The Borcherdt Malt Cod Liver Oil products contain the finest Norwegian Medicinal Cod Liver Oil of proven vitamin potency.

SAMPLE AND LITERATURE ON REQUEST

BORCHERDT MALT EXTRACT COMPANY
217 North Lincoln Street - - - CHICAGO, ILL.

Keeping faith with the Profession over a period of more than fifty years has been just one of the reasons why BORCHERDT'S MALT PRODUCTS are preferred by all who become acquainted with them

The Management of an Infant's Diet

Malnutrition, Marasmus, Infantile Atrophy, Athrepsia

Mellin's Food	**8 level tablespoonfuls**
Skimmed Milk (1% fat)	**9 fluidounces**
Water	**15 fluidounces**

This mixture contains 56.61 grams of carbohydrates, thus supplying material that is utilized rapidly for heat and energy. The predominating carbohydrate is MALTOSE, which has the highest point of assimilation of any of the sugars, is immediately available as fuel and may be safely given in comparatively large amounts. The daily intake of protein from the employment of this formula, is 15.54 grams, an amount calculated to be sufficient to replace depleted tissues and to provide for new growth. There is present in the mixture 4.32 grams of salts for replenishing inorganic elements.

The suggested modification furnishes nutrition in keeping with the character and amount of food elements best adapted to the particular demands of infants in an extreme state of emaciation and serves well as a starting point in attempting to meet the nutritive requirements of these undernourished babies.

Mellin's Food Co., 177 State Street Boston, Mass.

The Premier Digitalis

Digifoline, "Ciba"

The Digitalis which gives you results when others fail

According to actual experiences of physicians DIGIFOLINE, "CIBA" *will stand this test*

Physiologically Standardized

Tablets and Liquid

For Internal Use

TRADE C B A MARK REGISTERED

Ampules

For Subcutaneous and Intravenous Use

Ciba Company

INCORPORATED

CEDAR AND WASHINGTON STS. NEW YORK CITY